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TOPOGRAPHY AND PATHOGENESIS OF LESIONS IN RHEUMATIC FEVER.

BY

A. F. BERNARD SHAW, M.D.,

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In recent years interest has been revived in the pathological anatomy of rheumatic fever by the studies of MacCallum[1] on lesions of the left auricle and the series of papers by Pappenheimer and Von Glahn[2] on lesions of the aorta and other vessels. Indeed since the description of the specific nodes in the myocardium by Aschoff (1904) and Geipel (1905), it has become increasingly apparent that the cardiac lesions are merely local manifestations of a general infection, and that the more comprehensive our anatomical studies, the more fruitful are the results likely to be.

In a girl, aged 15 years, who died in December, 1927, of rheumatic fever with chorea the autopsy revealed extensive changes, and although the microscopic lesions were recognized at that time, unavoidable circumstances prevented a detailed study of the material until recently. Only those changes which prove the generalization of the infection and those which bear upon pathogenesis are discussed, the more commonly recognized lesions being briefly dismissed.

Pathological Report.

Autopsy protocol.—Rheumatic endocarditis of mitral and aortic valves with characteristic vegetations. Mitral leaflets thickened and rigid but no stenosis. Aortic cusps slightly thickened and opaque. Dilatation and hypertrophy of heart. Organizing pericarditis. Sero-fibrinous exudate of about 500 c.cm. in right pleural cavity. Left pleural cavity obliterated by delicate adhesions. Three subcutaneous nodules each about 3.0 mm. in size on right elbow. Chronic passive congestion of viscera.

On the cut surface of the left ventricle near its base are many opaque white points which proved to be Aschoff nodes histologically.

Of special interest are the appearances in the auricles. In the left chamber the endocardium of the posterior wall of the atrium for a distance of 3·0 c.cm. above attachment of mitral leaflet is roughened by numerous raised opaque yellowish flecks and ridges which assume a vertical direction and tend to fuse together as they approach the base of the valve where they merge with similar opacities in the substance of the leaflet. Similar lesions are scattered over the rest of the atrium and also in the appendix where they are vertically arranged over the musculi pectinati.

In the right auricle at the mouth of the coronary sinus and just above the attachments of the tricuspid valve are similar flecks and ridges. There are no vegetations on the thin and delicate tricuspid leaflets but beneath the endothelium are some yellowish opacities about 1.0 mm. in length extending down to the line of closure and lying with their long axes at right angles to the free margin of the valve.

The pulmonic valve appears normal but in the base of each cusp at its attachment to the arterial ring is a continuous line of yellowish opacity extending into the cusp for about 1·0 mm. The pulmonary artery with its main branches and the aorta throughout its whole length appear normal.

Histological Report.

Lesions of the aorta and pulmonary artery.—Topographically the lesions involve the pulmonary artery and its two main trunks but not the branches within the lungs; the ascending aorta, the arch, the descending thoracic but not the abdominal portion. The changes are more marked in the ascending aorta than in the other segments and less marked in the pulmonary artery than the ascending aorta. At these sites there is an inflammatory process in the adventitia and outer two-thirds of the media consisting of acute, healing, and healed lesions so dispersed that the appearances vary considerably in different parts of the same vessel. Acute lesions in the adventitia appear as infiltrations of mobile cells: lymphocytes, plasma cells, macrophages and many polymorphonuclear cells scattered diffusely through the tissue but also collected round the nutrient vessels (Fig. 1). The collagen bundles are often swollen and disintegrated and where this is so, isolated Aschoff cells are present but do not form nodes. In the nutrient vessels the endothelial cells are swollen and the walls turgid with œdema. At a later stage the polymorphonuclears have disappeared leaving the other types of mobile cells collected chiefly round the

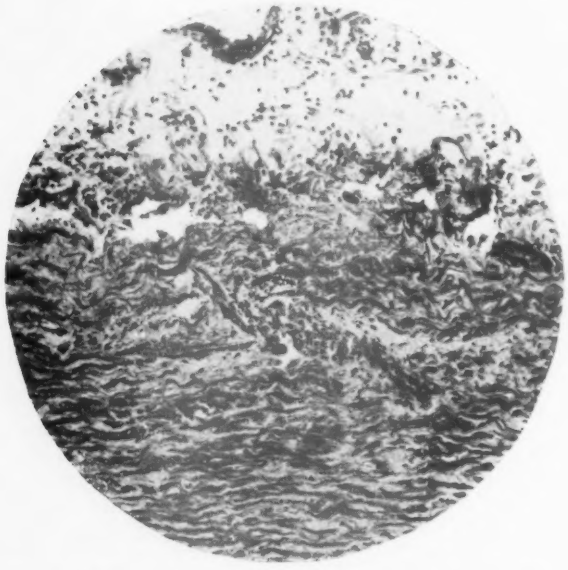

Fig. 1.—Pulmonary artery. Diffuse inflammatory cell infiltration in adventitia; extension of the process along a nutrient vessel into the media with destruction of the muscle fibres. × 90.

Fig. 2.—Ascending aorta. Showing proliferative endarteritis of a nutrient vessel in the adventitia and inflammatory cells round a nutrient vessel in media. × 40.

nutrient vessels which are greatly thickened by proliferative endarteritis (Fig. 2). Lenticular shaped Aschoff nodes in which the large Aschoff cells lie in a matrix of swollen necrotic collagen are occasionally found in these areas (Fig. 3). Healing is effected by the formation of dense nodular scars.

The changes in the media are essentially the same but their distribution is determined by the nutrient vessels which are enveloped by inflammatory cells (Fig. 1 and 2). There is destruction of the musculo-elastic elements of the media in these foci, so that when healing occurs the thickened nutrient vessel is surrounded by a nodular scar (Fig. 4). Isolated Aschoff cells are found in the fresh lesions, but no nodes are seen in the media. In only one instance is an intimal lesion found, and this occurs in the aorta immediately above its origin from the arterial ring. Here several Aschoff cells are arranged in a single row between the lamellæ of the subendothelial tissue; with them are some mobile cells, and cells with elongated twisted nuclei lying vertically to the surface of the aorta. As will be seen later the characters of this lesion are reproduced on a larger scale in the auricular endocardium.

Lesions of other vessels.—In the common carotid, subclavian and renal arteries, and superior vena cava, there is cellular infiltration of the adventitia and swelling of the nutrient vessels but the media and intima are intact. The cœliac axis presents a large lenticular scar in the middle of the media with thicknening of the overlying intima and inflammatory cells round the vasa of the subjacent adventitia (Fig. 5). The splenic and the superior mesenteric arteries and a main

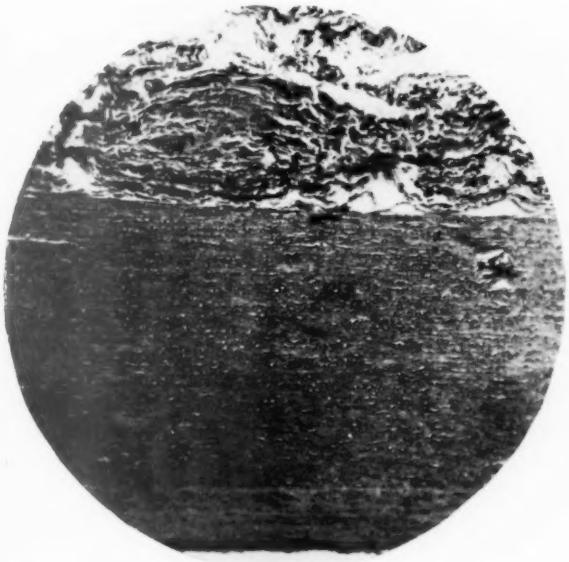

Fig. 3.—Descending thoracic aorta. Showing an Aschoff node composed of swollen collagen and large Aschoff cells lying in the adventitia. × 40.

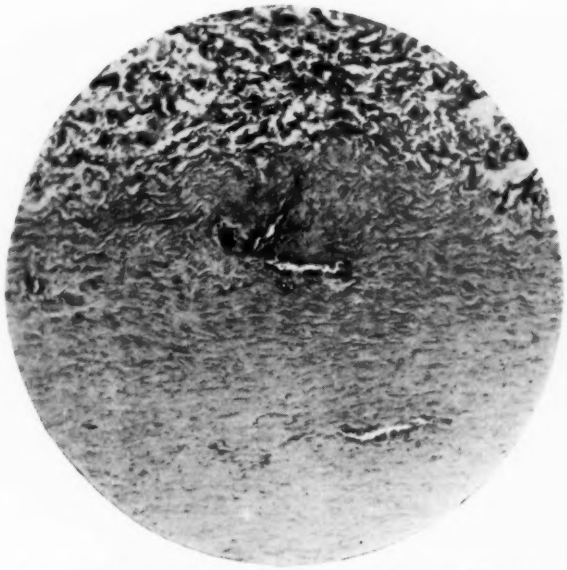

Fig. 4.—Pulmonary artery. Round a thickened nutrient vessel at junction of adventitia with media is a nodular scar. An active inflammatory focus about a nutrient vessel is seen deeper in the media. × 60.

Fig. 5.—Coeliac axis. A large elliptical scar in the media is covered by thickened intima. ×40.

Fig. 6.—Showing a venule in wall of left ventricle. About half the circumference of the vessel is infiltrated in all its coats by polymorphonuclear leucocytes. The intima is intact and there is no thrombosis. × 140.

pulmonary vein are quite normal and no vascular or other specific lesions are found in the liver, spleen, kidneys, lungs, uterus, ovary, oviduct, pancreas, thyroid, adrenal, urinary bladder, bone-marrow and rib.

There is commonly found, however, an acute type of vascular lesion affecting venules and less frequently arterioles situated in the myocardium, atrio-ventricular sulcus, the connective tissue between the auricles and arterial trunks and the superior mediastinum. It consists of swarms of mobile cells, chiefly polymorphonuclear, which infiltrate the adventitia and extend through the necrotic media to the intima where the endothelial lining remains unbroken but is raised up like a blister over the cellular exudate (Fig. 6). Usually only a sector of the wall is involved, more rarely the whole circumference. The most striking feature of this reaction is the absence of thrombosis although specific stains reveal abundant fibrin beneath the endothelium and outwards into the adventitia.

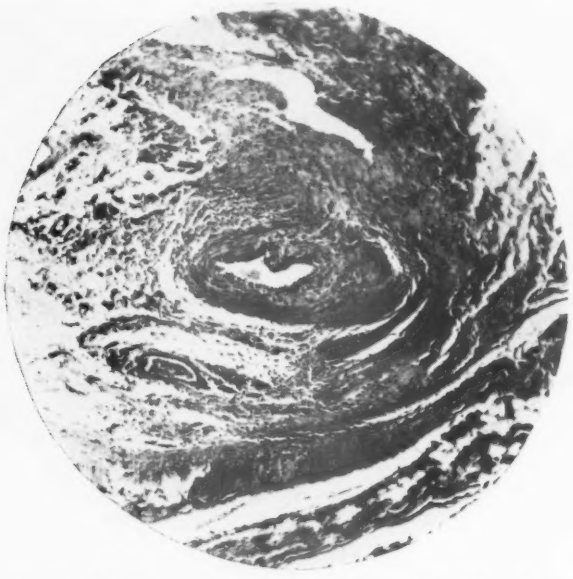

Fig. 7.—Diaphragm. Showing great scarring of the adventitia and media at one pole of an artery. Below this artery is an Aschoff node lying near a smaller vessel. × 60.

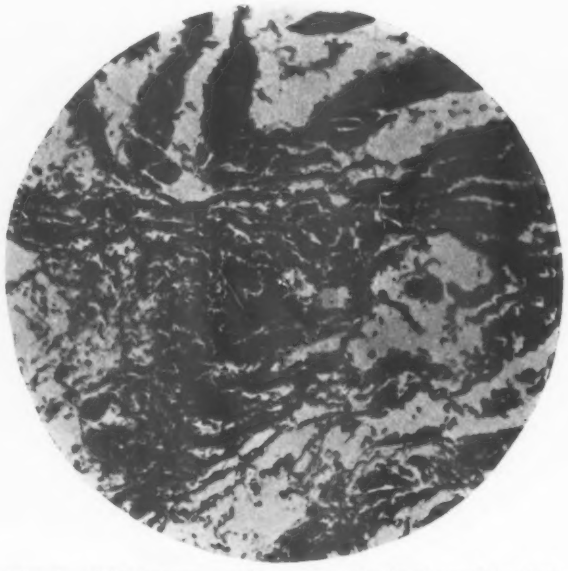

Fig. 8.—Diaphragm. A large irregularly-shaped Aschoff node situated at the junction of muscle with tendon. × 80.

Lesions of muscles.—The musculature of the soft palate and tongue and the hyoglossus muscle reveal no abnormality, but changes are present in the diaphragm and the superior constrictor of the pharynx where it is attached to the fibrous capsule of the tonsil. In the diaphragm the lesions present a definite relation to two structures, namely, the vessels and the connective tissue sheath which envelops the tendon bundles at their junction with the muscle fibres. A healed vascular lesion is shown in Fig. 7. where an artery is greatly thickened at one pole by dense scar tissue in the adventitia and media. Small Aschoff nodes are also found in the walls of the vessels. At the musculo-tendinous junctions in the connective tissue sheath there are either focal acute exudative lesions in which polymorphonuclear cells predominate or large Aschoff nodes of irregular outline (Fig. 8). In both forms of reaction the collagen fibres are swollen and necrotic but the tendon bundles are spared. The muscle of the superior constrictor of the pharynx is intact, but in the outer layer of the fibrous capsule of the tonsil to which the muscle fibres are attached there are a few Aschoff nodes (Fig. 9). Localizations of this kind suggest that the virus of rheumatic fever has a special affinity for the connective tissue sheath of tendon and aponeurosis, and for connective tissue to which muscle is attached. Confirmation of this view is derived from the numerous subendothelial lesions present at the junction of the chordæ tendineæ and papillary muscles, and the marked reaction in the connective tissue

sheath of the aponeurosis beneath the subcutaneous nodules of the elbow. In these parts too, the tendon and aponeurosis escape the injury which is located in the connective tissue envelop alone. Similarly the lesions at the insertion of the pharyngeal muscle may be compared as regards position to the annulus fibrosus of the heart which is greatly thickened by scar tissue, diffuse inflammatory infiltration and Aschoff nodes, while at the junction of the auricular and ventricular musculature with this structure Aschoff nodes are in evidence. Further, it seems probable that a topographical survey of the subcutaneous nodules in cases of rheumatic fever would show that their distribution is largely determined by this peculiarity. Of course, the specific nodes are not confined to the vicinity of tendon or aponeurosis, but wherever they occur there is always connective tissue. Indeed, the matrix of the node is always necrotic collagen which seems to constitute the initial and fundamental injury produced by the rheumatic virus, the cellular reactions being secondary. A study of numerous nodes in this case with specific

Fig 9.—An Aschoff node in the connective tissue between tonsil (above) and the superior constrictor muscle of the pharynx (below). × 75.

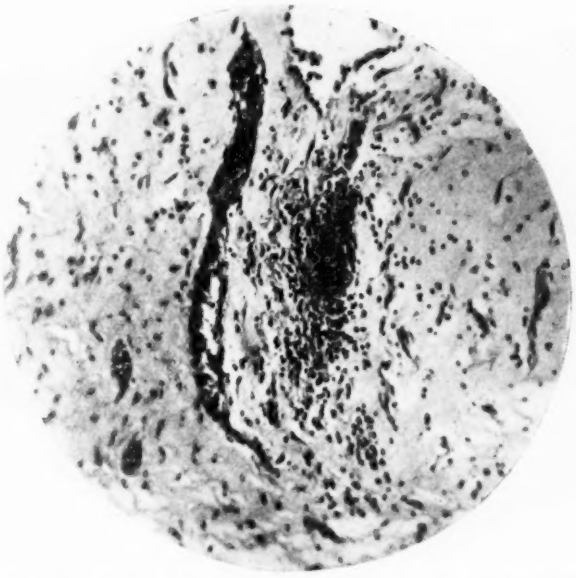

Fig. 10.—Visceral layer of pericardium. Showing an Aschoff node in the young granulation tissue of the organizing pericarditis. × 80.

stains gives no support to the idea that a deposit of fibrin forms the essential basis of the reaction because this material is seldom abundant in amount and is often absent even in fresh nodes. Nor does the reaction always appear as a node; sometimes as in the auricular and ventricular endocardium, intima of aorta, visceral pericardium, the Aschoff cells are arranged in rows along bands of swollen collagen suggesting that the actual shape of the lesion depends on the texture and stratification of the affected tissue.

Lesions of serious membranes and lymphoid tissue.—In the visceral layer only of the pericardium there are a few characteristic nodes in the young granulation tissue (Fig. 10) and in the fibrous pericardium itself small collections of Aschoff cells arranged in rows along swollen collagen fibres. The right parietal pleura exhibits an organizing exudate without nodes but, curious to say, the visceral layer shows no trace of inflammation. In the lymphoid tissue (tonsil, cervical, tracheo-bronchial, mesenteric, retro-peritoneal lymph nodes, splenic lymphoid nodules) there are many plasma cells—probably a response to the demand for these cells in the lesions elsewhere; and contrary to what is found in most infective conditions in young people the germinal centres of the lymph follicles are absent or inconspicuous.

Brain.—No adequate anatomical basis for the chorea is found in the meninges, cerebral cortex, caudate nucleus, corpus striatum, optic thalamus, mesencephalon and pons. All these show hyperæmia but no vascular or inflammatory lesions.

Certain cardiac lesions.—Nodes are sown thickly in the walls of both ventricles, those beneath the endocardium being covered by unbroken endothelium without thrombosis on the surface. In the atrio-ventricular sulcus are many lesions in various stages of evolution : nodes where the sulcus adipose tissue joins the annulus fibrosus ; fresh and resolving nodes in and about the coronary sinus and the right and left coronary arteries. Some sections show that healing has occurred in the circumflex branches of the coronary arteries so that the intima is greatly thickened and the media deeply scarred, the appearances being like those in arterio-sclerosis. Similar changes are present in the connective tissue filling the space between the auricles, aorta and pulmonary artery. On comparing the two sides of the heart it is seen that the sulcus lesions are symmetrically arranged, and the same phenomenon comes out in other situations, namely,

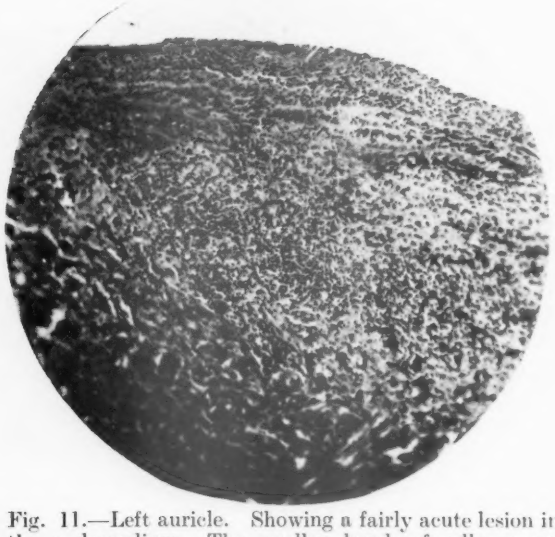

Fig. 11.—Left auricle. Showing a fairly acute lesion in the endocardium. The swollen bands of collagen are bordered by rows of large darkly stained Aschoff cells. There are many inflammatory cells near the surface and also in the outer part of the endocardium down to the muscle. Endothelium intact and no thrombi on surface. × 40.

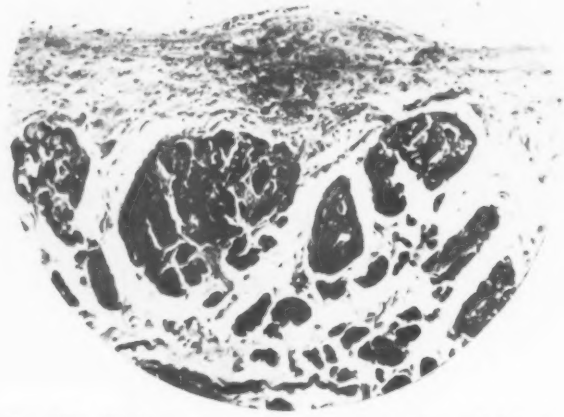

Fig. 12.—Right auricle. Showing an endocardial lesion which is resolving. Numerous large Aschoff cells lie among the swollen collagen fibres. Inflammatory cells have nearly all disappeared. × 120.

at the angle of attachment of the tricuspid and mitral valves to the annulus fibrosis and where the aortic and pulmonic valves spring from the arterial rings (Fig. 14). The changes in the auricular endocardium, more marked in the left than the right chamber, explain the gross appearances. Acute healing and healed lesions are found side by side. In the acute phase the endothelium is raised up and the subendothelial tissue inside the elastic lamina is much infiltrated with fluid and exudative cells, among which are many polymorphonuclears and cells with elongated twisted nuclei lying perpendicular to the surface. The collagen fibres inside and outside the elastic lamina are transformed into broad hyaline bands along which large Aschoff cells are arranged in rows like a palisade. The outer half of the endocardium down to the muscle is swollen with fluid and infiltrated by many wandering cells chiefly of mononuclear type (Fig. 11). There is no fibrin deposit on the surface of the unbroken endothelium. As resolution takes place the exudative cells disappear leaving the swollen collagen fibres and the Aschoff cells (Fig 12.). Healing occurs readily. Young scar tissue of delicate collagen fibrils and vertically orientated fibroblasts is formed inside the elastic lamina where it appears as a cushion-like swelling covered by intact endothelium (Fig. 13).

The Mechanism of Rheumatic Endocarditis.

Koster (1878) appears to have been the first to suggest that endocarditis was embolic in origin rather than due to the implantation of bacteria on the surface of the valve from the passing blood. For many years his theory met with opposition owing to uncertainty regarding the presence of blood vessels in the normal valves of the adult. However in 1917 Bayne-Jones[3] was able to demonstrate by injection methods a vasculature in the valves of normal hearts. He found that the mitral and tricuspid valves receive arterioles from the coronary arteries as they pass through the annulus fibrosus. These arterioles penetrate the base of the leaflet and pass downwards giving off small lateral branches which ramify in the upper third. When they reach the line of closure

Fig. 13.—Left auricle. Representing a healed endocardial lesion which is seen as a cushion-like swelling of young scar tissue. This rests upon several layers of swollen collagen between which are many Aschoff cells in rows. × 40.

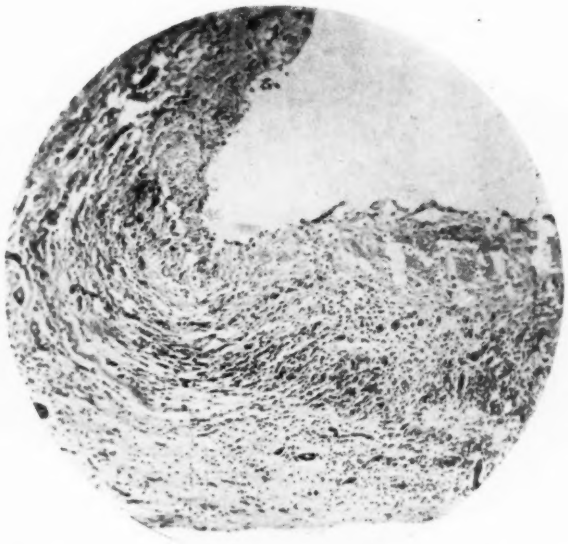

Fig. 14.—Pulmonary valve. Showing base of valve (below) at its attachment to the arterial ring (above). At the angle so formed is a small Aschoff node beneath the endothelium. The base of the valve is the site of an inflammatory reaction, Aschoff nodes and new-formed vessels. × 40.

they undergo multiple branchings forming tufts of vessels in this region with an abundant capillary anastomosis. Only occasional strands pass from the line of closure into the filamentous edge of the valve. He also found that delicate strands of vessels pass up along the chordæ tendineæ almost to their insertion into the valve, but he failed to detect an anastomosis between these vessels and those in the valve. However, Wearn[4] in the self-perfused human heart saw the vessels in the chordæ tendineæ enter the valve.

The semilunar valves receive a blood-supply from the nutrient vessels of the pulmonary artery and the aorta and from vessels of the auricular endocardium. The few delicate vessels which arise from the nutrient vessels where the valve is attached to the wall of the artery, penetrate the valve for a very short distance along its line of closure. The auricular vessels form a hedge-like

plexus in the base of the cusp, and from this plexus delicate vessels pass upwards for a distance of about half the cusp, the rest of the cusp being devoid of vessels.

In the light of Bayne-Jones's work the changes in the tricuspid and pulmonic valves of the present case are suggestive, because they indicate the mechanism by which endocarditis and valvulitis are produced in rheumatic fever. It is important to note that there is no endocarditis of either valve and no evidence that this condition has ever been present. In about the proximal quarter of the pulmonic valve there is a characteristic inflammatory reaction with Aschoff nodes and new-formed thickened vessels (Fig. 14) which are continuous with lesions in the arterial ring. The rest of the valve out to its edge is normal and covered by unbroken endothelium. In the tricuspid leaflets

Fig. 15.—Tricuspid valve. (Proximal third). The circumscribed rounded body in centre of valve tissue is a resolving Aschoff node. A number of thickened arterioles lie to the right of the node. × 40.

Fig. 16.—Tricuspid valve. (Near line of closure). Showing a subendothelial recent Aschoff node covered by intact endothelium. There is diffuse cellular infiltration in thickened tissueof valve. × 40.

there is a diffuse valvulitis, acute healing and healed lesions being present from the base to the line of closure. Compared with a normal valve the whole leaflet is thicker and of coarser texture as if from diffuse scarring. In the basal portion are many new-formed thickened arterioles (Fig. 15) and capillaries extend down to the line of closure. Deep in the substance of the proximal portion is an Aschoff node (Fig. 15) and foci of inflammatory cells are scattered as far as the line of closure. On the auricular and ventricular faces of the leaflet are subendothelial nodes (Fig. 16), one of which near the line of closure has healed, producing a cushion-like swelling similar to the healed lesions in the auricles. This entirely confirms the opinion of Coombs, Swift and others, that in rheumatic fever valvulitis rather than endocarditis is the essential lesion. Yet comparison of the two valves shows that the extent of the valvulitis is different; in the pulmonic only the basal part is involved, in the tricuspid

the whole length. This difference is governed, we believe, by the degree of vascularity. In the tricuspid, diffuse permeation with the virus occurs readily owing to the good blood-supply, and the opportunities for re-infections are increased by the healing of the inflammatory process which leads to the formation of new vessels from the pre-existing ones. In the pulmonic valve the initial infection only injures the basal sector, and since the spread of inflammation into the distal non-vascular area takes place by continuity its progress must be relatively slow.

As regards endocarditis, it has always been a matter of dispute whether destruction of the endothelium is primary or subsequent to an injury of the underlying tissue. In this connection it may be said that the rheumatic virus is not readily a thrombogenic agent, as is shown by the fact that lesions immediately beneath the mural endocardium and the intima of vessels are rarely accompanied by thrombosis—a peculiarity which also impressed von Glahn and Pappenheimer in their study of vascular lesions. Yet vegetations are almost constantly found on one or more valves in rheumatic fever, showing that some other factor must be acting in conjunction with valvulitis. As is well known, endocarditis appears along the line of closure of the valve, being rarely seen elsewhere. Now the line of closure is a zone in which mechanical stress is considerable when the leaflets come into apposition and a locus minoris resistentiæ is present in this position, so that endocarditis develops here and not elsewhere on the leaflet. But while mechanical stress alone seems to determine the location of endocarditis it does not by itself explain the relative frequency of endocarditis of the different valves. If it were the sole factor then endocarditis should involve the left heart more than the right, the mitral as often as the aortic and the tricuspid as often as the pulmonic. However, it is known that rheumatic endocarditis involves the valves in the following order of frequency—mitral, aortic, tricuspid, pulmonic. If, however, we consider the degree of vascularity of a valve as acting in conjunction with the amount of mechanical strain imposed on it, then these two factors afford a reasonable hypothesis to explain the relative frequency of endocarditis of the four valves (see Table).

TABLE.

Illustrating Factors responsible for the Relative Frequency of Endocarditis of the Different Valves in Rheumatic Fever.

Valve.	Mitral.	Aortic.	Tricuspid.	Pulmonic.
Frequency of endocarditis	+ + + +	+ + +	+ +	+
Amount of strain	+ +	+ +	+	+
Amount of vasculature	+ +	+	+ +	+

From the study of the case reported here it seems quite clear that valvulitis precedes endocarditis, and that probably the latter cannot develop until the inflammatory process has permeated the leaflet as far as the line of closure.

That the valvulitis can be of considerable extent and severity before endocarditis occurs is shown by the tricuspid valve, in which the anatomical conditions indicate repeated infections of the valvular tissue without the production of endocarditis before death.

It would be interesting to know how often valvulitis as distinct from endocarditis occurs in rheumatic fever, because it is evident that valves without endocarditis and otherwise normal on naked eye inspection cannot be acquitted of extensive inflammation until examined by the microscope.

My thanks are due to the Newcastle-upon-Tyne and Northern Counties Medical Society for a contributory grant from its Research Fund in aid of expenses incurred in this investigation.

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EXTENSIVE VISCERAL ENDARTERITIS OBLITERANS IN A YOUNG CHILD.

BY

JOHN McMICHAEL, M.B.,

(From the Paddington Green Children's Hospital, London.)

The following case seems worthy of record on account of the baffling clinical picture and the unique post-mortem findings. The illness occurred in a child of eighteen months, the main clinical features being general malaise and fretfulness, fever and some gastro-intestinal disturbance. Death was caused by thrombosis of the superior mesenteric artery. At autopsy a generalized visceral endarteritis was found with infarcts in various organs.

Bernard H., aged eighteen months, was admitted to the Children's Hospital, Paddington Green on September 7th, 1928.

About the first week of August, 1928, he had developed a scarlatiniform rash which disappeared in two days. He had vomited once at the onset but there was no sore throat and he had not appeared ill. The condition was probably a toxic erythema and not scarlet fever.

He remained fairly well until September 2nd, when he lost his appetite, became listless and seemed to have no energy. Motions became slimy but there was no actual diarrhœa. On the evening of his admission to hospital he vomited four times, the vomit being greenish and watery with mucus. There was a history of slight cough for some weeks.

Previous health and family history.—The child had been previously healthy and there was no history of any preceding infectious or other diseases.

The father and mother, both aged thirty, were well. The Wassermann reaction (taken later) was negative in both. Their first child, a girl, had died of tuberculous meningitis when four years old. The second child was premature and died when a few days old. Present case was the third child. The family was not Jewish. Home conditions were good, the family living in moderately comfortable circumstances in the country.

On admission.—A pale, anæmic, listless child weighing 21 lb. 4 oz. Temperature 101.6°; Pulse 110–140 per minute. There was no throat or middle-ear infection. A few slightly enlarged cervical glands were felt. There was slight tenderness in both iliac fossæ but apart from this there were no abnormal physical signs. The lungs were clear. The heart was not enlarged and sounds were closed. The spleen and liver were not enlarged. The urine contained no abnormal constituents and there was no sign of disease in the central nervous system.

During the three days following admission the child was very miserable and unhappy. His temperature fell to normal, but he was passing two or three loose, offensive stools each day. Owing to his fretful state the parents insisted on taking the child home on September 11th.

At home the temperature was taken daily and it ranged from 98°—99° in the morning to 101°—102° in the evening. Progress was variable. On some days he was quite bright especially in the mornings, but he was always tired in the evenings; on other days he was very listless all day. There was no further diarrhœa, but stools were offensive and dark-coloured, and he continued to vomit about one or twice a week.

On October 3rd, 1928, the child was readmitted to the hospital. Weight was 21 lbs. 2 oz. (*i.e.*, practically stationary as compared with weight a month previously). Examination revealed, in addition to the previous findings, that one or two glands were palpable in the right iliac fossa. The von Pirquet test was strongly positive. X-ray examination showed a slight increase of fibrous tissue about the hila of both lungs.

Blood Condition.—Red blood corpuscles 4,580,000 per cmm., leucocytes 16,000; hæmoglobin 60 per cent., colour index 0.66. Many poikilocytes present. Differential count:—polymorphonuclears 64 per cent., lymphocytes 26.6 per cent., hyalines and transitionals 8.4 per cent., eosinophiles 1 per cent., basophiles not found.

The stool shewed no occult blood and the bacterial content was normal. The temperature continued to swing from 99° to 102°.

A clinical diagnosis of glandular tuberculosis was made. On open-air treatment and careful dieting he gained a pound in weight during the next ten days.

On October 16th, he passed a very loose, dark, foul-smelling stool containing mucus and pus—the latter obvious to the naked eye. The temperature rose to 104° and then slowly settled down in the next twenty-four hours. Palpation of the abdomen and rectal examination revealed nothing. It was surmised that a softened gland might have ruptured into the bowel. Examination of the stool revealed blood and pus. Culturally B.coli and streptococci were found in normal proportions and there was obtained a free growth of a bacillus having the characters of B.dysenteriæ (Sonne). The amount of pus, however, was too abundant for the case to be regarded as one of dysentery only. For the next few days stools were loose and offensive with a little mucus.

At midday on October 26th, he made himself sick by pushing his fingers down his throat. Shortly after this he was found with a little very slightly blood-stained mucus on his pillow, the source of which could not be determined. The child looked pale and anxious: temperature fell from 101° to 96° and the pulse rose from 110 to 144 per minute. No physical signs could be elicited in the chest or abdomen. The whole picture was one of shock and no evidence of internal hæmorrhage could be found. He was seen by a surgeon who was not inclined to interfere. At 11 p.m. the abdomen began to become distended but there had been no further vomiting. Between 11 p.m. and 3 a.m. he vomited thrice and death took place at 3 a.m. on October 27th, 1928.

Post-Mortem Report.

Only an abdominal incision was permitted. On opening the abdomen a little blood-stained fluid escaped and plum coloured coils of small intestine, markedly distended with gas, presented in the wound. These coils consisted of several feet of ileum. The peritoneal surface was smooth and glistening but a few flakes of lymph were occasionally encountered. There was no evidence

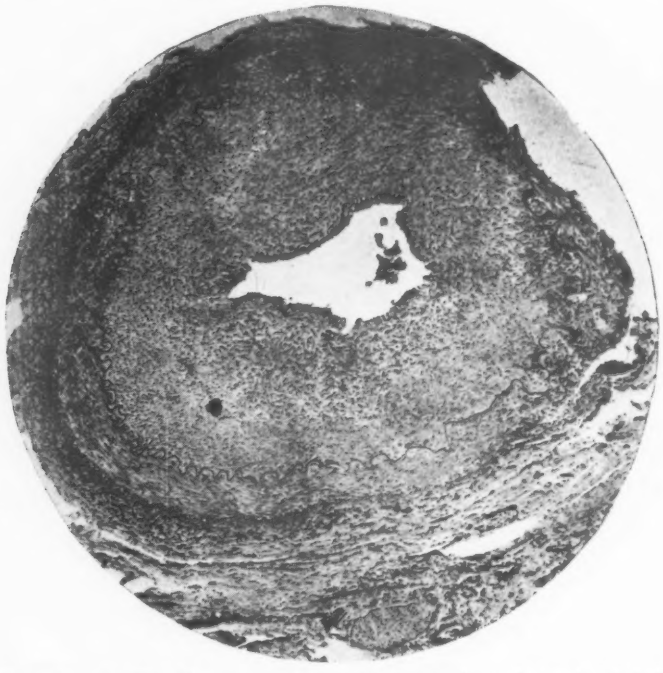

FIG. 1. × 75. Cross section of descending branch of left coronary artery, showing great connective tissue proliferation in the intima.

of ulceration in either the small or the large bowel. A few enlarged and slightly caseous glands were present in the mesentery near the cæcum.

The spleen was small and firm ; along its borders were found five infarcts—some recent, others white in colour and older. The liver was normal. In the kidneys many infarcts were present in both—more numerous in the left kidney (5) than in the right (2). As in the spleen, some were recent and others of longer standing.

The heart was not enlarged. The muscle wall was rather flabby. The coronary vessels were very prominent and of opaque white colour—they felt like dense fibrous cords. Their walls were very definitely thickened and the lumen of the artery extremely narrowed. In the wall of the left ventricle was one firm dense white fibrous patch and a few smaller areas of patchy fibrosis were found towards the apex. None of these fibrotic areas involved the endocardium and there was no ante-mortem thrombus formation in the heart. The valves were normal.

In the lungs all lobes presented on the surface small soft hæmorrhagic and plum coloured areas which appeared to be infarctions. In one or two of these the centres were softening but there were no definite abscesses.

The aortic wall was smooth and presented no atheromatous changes. The mouths of the coronary arteries were not involved.

Microscopical examination.—Sections were made from the heart wall, kidney and spleen. The most notable and the primary change in all these organs was endarteritis obliterans of the small arteries. It is worthy of note that although the descending branch of the left coronary artery and other arteries of a similar size were heavily involved, the smaller arterioles were not affected.

The affected vessels shewed great connective tissue proliferation internal to the internal elastic lamina, with great narrowing of the lumen (Fig. 1). In some sections thrombosis was observed. The media and adventitia were quite normal. The vasa vasorum shewed no perivascular leucocytic infiltration. The results of this obliterating and thrombotic process were visible in the organs examined. In the heart wall, loss of muscle tissue and replacement fibrosis were seen (Fig. 2).

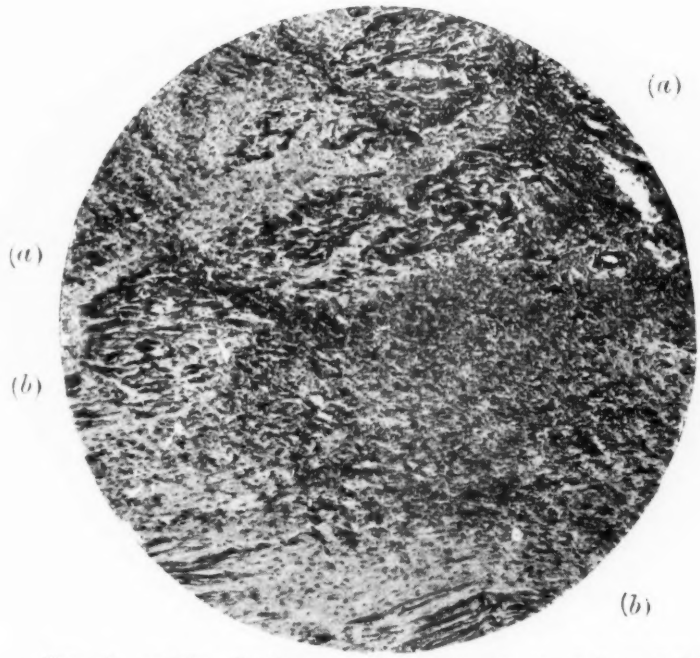

FIG. 2. × 100. Section of the wall of the left ventricle showing loss of muscle fibres (*a*) and replacement fibrosis (*b*).

In the kidney and spleen necrotic areas were present, characterized by loss of structural outlines in the cells and pyknotic nuclei. In the middle of one such area in the kidney an affected vessel was seen containing an organized thrombus.

Discussion.

The pathological condition described must be termed endarteritis obliterans. Thrombo-angiitis obliterans and polyarteritis nodosa are excluded by the complete absence of any involvement of the adventitia : the herniations of the muscular coat and the aneurysms of the latter condition were completely absent.

On reviewing this case it is realized that the clinical manifestations must, of necessity, be exceedingly protean. Even had the underlying pathological condition been suspected during life it is difficult to see how the diagnosis could have been made, as it is quite impossible to point to any single pathognomonic feature.

It must be assumed that the process of proliferation of the intima had been going on for many weeks before the child's death, and that from the time he came under observation small thrombotic accidents were occurring from time to time right up to the final catastrophe of mesenteric thrombosis which caused his death. The disturbance caused by these events would certainly be sufficient to account for the general malaise and fretfulness which were such prominent features. Had the patient been older, the onset of more or less severe pain might have been determined in various parts of the body where the infarctions took place. The occasional vomiting and the passage of loose stools may have resulted from small infarctions involving the bowel wall. The vomiting also may have been a reflex phenomenon resulting from infarctions in any of the abdominal viscera. The absence of any physical signs is easy to understand, for the infarctions were never bigger than a pea. Had the urine been examined fully every day some evidence of renal infarction might have been found. A friction rub might also have been heard had a daily examination of the chest been carried out with sufficient zeal. It is worthy of note that there were no attacks of dyspnœa or cyanosis such as are found in the well defined group of cases of pulmonary arteritis in children[1]. It is quite possible that slight hæmoptysis occurred the day before death took place.

The occurrence of fever was a striking phenomenon throughout the illness, and almost certainly was more of the nature of a causal factor than the direct result of the arterial disease.

In considering the ætiology the question of hereditary syphilis arises. Clinically there were no grounds for any suspicion of this disease and it was only after death that the Wassermann reactions were taken in both the father and mother, with a completely negative result. In syphilis and tuberculosis, endarteritis obliterans is common in the neighbourhood of local lesions (*e.g.*, gummata and lung cavities). Generalized visceral endarteritis unassociated with local lesions must be exceedingly rare. In syphilis it occurs in the blood-vessels of the brain apart from local lesions. In the present case there was no clinical evidence of any involvement of the cerebral arteries, but owing to the limited post-mortem this was not confirmed. Fremont Smith[2] in a critical

review of arteriosclerosis in the young states that 'the role of congenital syphilis has been overestimated in youthful cases by earlier writers who were not aware of the part that acute infections play.' He demonstrates that in most of the recorded cases evidence of syphilis was wanting.

Evidence of tuberculous infection was present in the case under discussion in the form of a positive Pirquet reaction and slightly enlarged caseous glands. The possibility that this was an ætiological factor cannot be overlooked but this theory seems untenable for two reasons. First, the frequent incidence of tuberculosis stands in marked contrast with the extreme rarity of the arterial disease under discussion. Secondly, when the arteries are attacked in general tuberculosis the lesion is a definite tuberculous arteritis and totally different from the present arterial disease. One further point is that the child did not belong to the Jewish race, which seems, for some unknown reason, more prone to arterial disease in early life.

The condition must therefore be regarded as a visceral endarteritis due to an acute or subacute infective process of an unknown nature.

In conclusion I have to express my gratitude to Dr. F. Parkes Weber for his kindly interest and to Dr. Reginald Miller for permission to publish the case.

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STUDIES OF PNEUMONIA IN CHILDHOOD.

IV. BRONCHIECTASIS AND FIBROSIS OF THE LUNG.

BY

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It is stated that Laennec was the first to describe the condition of bronchiectasis, although fibroid conditions of the lung were described by earlier morbid anatomists.

In " De L'Auscultation Mediate " (1826) Laennec[1] has a short chapter entitled ' Dilatation of Bronchi,' in which he gives the history, the clinical condition and the morbid anatomy of four cases. In three of these the origin of the condition was apparently in childhood. One was a child of three years who died three months after whooping cough. Another was a man in middle life, who ' from infancy was subject to a cough attended by an expectoration of yellowish or greyish colour : this had not in any way prevented him from following his occupation.' The third was an old piano teacher, ' aged seventy-two years, affected upwards of fifty years with habitual cough, expectoration of opaque yellow sputa, and short oppressed breathing. However, she was always able to attend to her affairs, and indeed never considered herself as sick.' Laennec goes on to describe minutely the bronchial dilatations, and the dense contracted condition of the lung substance which he refers to as ' a cartilaginous production extending from the bronchial walls into the substance of the lungs'. His account of the subject is not only important historically : it is still useful, sound and accurate. Later reports of bronchiectasis confirm his findings of a condition dating back to childhood in a majority of cases ; compatible not only with long life but even with moderate health and capacity for work ; and dependent on bronchial dilatation associated with pulmonary fibrosis. His theory of ætiology is also worth quoting : it is ' a temporary dilatation produced by a voluminous sputum, and is rendered permanent by the constantly successive secretion of similar ones'.

Corrigan's[2] paper on ' Cirrhosis of the Lung ' in 1838 is the next important contribution to the subject. He reported four cases. As his title indicates, Corrigan regarded the fibrous change in the lung as the primary condition, which produces by traction the dilatation of the bronchial passages. This explanation of bronchiectasis obtained and still obtains much support.

For a long period, there was confusion between cases of true bronchiectasis and of tuberculous cavitation : and until the demonstration of tubercle bacilli in sputum was possible, the separation of the two conditions was difficult. But in 1891 Clark, Hadley and Chaplin[3] reported 45 cases of bronchiectasis under the descriptive term ' fibroid lung ' : and in all these a tuberculous condition was excluded by repeated examination of the sputum. In contrast to the small series of Laennec and Corrigan, the majority of these 45 patients were alive and ' in the enjoyment of excellent health'. Another important feature of the series was that, although only eight of the cases were under ten years of age, in the great majority the originating illness had occurred before the age of five years. In 33 the condition had followed measles or whooping cough or both.

In 1905 Clive Riviere[4] published an analysis of 33 cases, all in children, with 3 autopsies. In 23, the original illness occurred under 5 years of age : in nearly all it was of the nature of bronchitis or broncho-pneumonia, and was especially associated with measles and whooping

cough. The title of his paper was 'Pulmonary Fibrosis in Childhood', but he declared that bronchiectasis was an invariable accompaniment. In 4 cases he believed the cause to have been an unresolved apical lobar pneumonia.

In 1927 Findlay and Graham[5] reported 23 cases of definite bronchiectasis in childhood. This paper was particularly valuable in giving a number of lipiodol radiographs of the lungs, showing accurately the extent and character of the bronchial dilatations. Again in a majority of these cases, the original illness was bronchitis or broncho-pneumonia, often associated with measles and whooping cough: although in two cases the primary condition was pleurisy, and in three no originating acute respiratory illness could be traced.

This brief historical survey brings out several interesting points. Bronchiectasis was first discovered and described in the post-mortem room, many years after the process had begun: it was next studied during life, but still at an advanced stage. Also the great majority of the reported cases indicated as the original cause an acute respiratory illness in early childhood. Since 1900 careful studies of cases in children have been made, but it is uncommon to find reports of cases where the condition had been observed from its beginning, although Findlay and Graham were able to observe three 'almost from the beginning', following respectively double pleurisy, broncho-pneumonia and lobar pneumonia. Lastly, bronchiectasis was so commonly associated with fibrosis of the lung that the latter condition received an important place in the terminology, as shown by the terms 'cirrhosis of the lung', 'fibroid lung', and 'pulmonary fibrosis'.

In the first paper of these 'Studies of Pneumonia'[6], we referred to a group of 33 cases of 'bronchiectasis' following pneumonia and bronchitis, which have been under our observation. This group was a composite one, including definite cases of bronchiectasis with or without fibrosis of the lung, and an indefinite group where physical and X-ray examination was inconclusive of either bronchiectasis or fibrosis. Yet in this indefinite group, the chronic and special character of the bronchitis and the history of an originating pneumonia or bronchitis seem to justify the diagnosis of some fibrous change in the bronchi and the interstitial stroma of the lung. Some years ago, before the introduction of lipiodol, one of us (C. McN.[7]) reported 18 cases of 'fibrosis of the lungs and bronchi, following broncho-pneumonia', of which only 6 were of definite or massive fibrosis; while in the remainder the fibrosis was indefinite, although the clinical character of the cases in both groups was similar. The subsequent use of lipiodol in some cases of the indefinite group has demonstrated in them bronchial dilatation, and it is possible that this method may reveal some degree of bronchiectasis in many cases of chronic cough and spit following broncho-pneumonia. Certainly the use of lipiodol has shown beyond doubt that definite bronchiectasis may exist without producing either the classical physical signs or evidence in an ordinary radiograph.

From all these data, it would seem that the majority (probably the great majority) of cases of bronchiectasis date back to early childhood and originate in broncho-pneumonia or bronchitis. It might be hoped, therefore, that microscopic study of the bronchial changes in acute and chronic cases of broncho-pneumonia would throw light on the origin of bronchiectasis. The main

purpose of the present paper is to present such a microscopic study of a series of cases of broncho-pneumonia, and of early and advanced bronchiectasis.

As an introduction to this study, it may be of interest to give a short clinical record, with lipiodol X-ray photographs, of two cases of bronchiectasis, in both of which the condition is definite, has existed for some years and has permitted fairly good general health.

Clinical Case A. John M., present age 7 years. Admitted to hospital in the fifth week of double broncho-pneumonia following measles, at the age of 2½ years. The boy was wasted very weak and pale, and in an extremely grave condition. His lips, tongue and mouth were covered with numerous dirty ulcers; these involved the larynx also, as shown by his complete

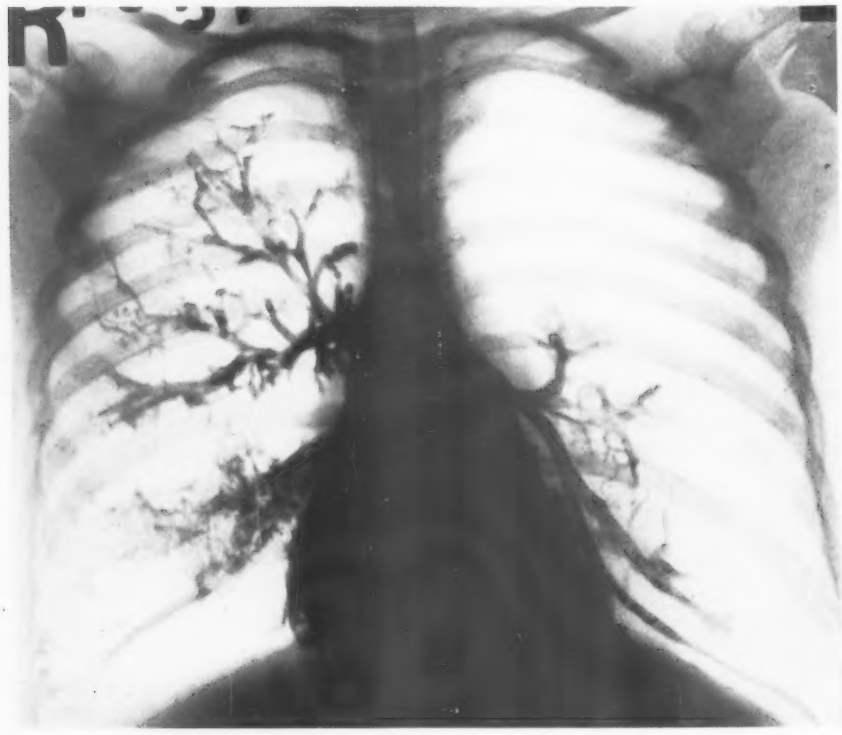


FIG. 1.

aphonia. There was irregular and patchy consolidation of both lower lobes; radiographs confirmed the pneumonic condition of the lungs. He slowly improved, and remained in hospital for twenty weeks. His recovery was marked by persistent and paroxysmal cough, which had not entirely left him on his discharge. His general health was then excellent. His cough became worse again in the following winter, and was of the typical paroxysmal "morning cough" type, with the expectoration of a moderate amount of purulent but not offensive spit. It remained, with exacerbations and improvement, until his re-admission at the age of 5½ years. His general health had kept fairly good: he was never in bed, and he had gone to school. On re-admission, his colour was good, his nutrition fairly good: there was very slight clubbing of the fingers. His lungs showed no percussion dulness: but there were numerous hollow-crackling rales at both bases, with broncho-vesicular breathing at these areas. The ordinary radiograph of the lungs showed luminous fields: but the cardiac shadow was overlaid with an indistinct tracery which suggested thickened bronchi. The lipiodol-radiograph showed a definite bronchiectasis

at both bases close to the spinal column : and on the left side one or two slightly widened bronchial tubes could be seen passing across to the periphery above the dome of the diaphragm. (Fig. 1.) He is again under observation, æt. 7 years, four and a half years after his original pneumonia : the condition of bronchiectasis has not apparently progressed : cough and spit remain as before : the general condition is fairly good : the boy is able to attend school, and to play.

Commentary. A case of limited bilateral bronchiectasis, without massive fibrosis of the lungs, following measles and broncho-pneumonia. General health fairly good. Duration, 4½ years.

Clinical Case B. Jessie W., present age 14 years. She had measles and pneumonia at the age of 3 years, and was said to be seriously, but not dangerously, ill for several weeks. She was not under our observation during this illness. Since this time, she has never been free from cough : she has bouts of cough every morning on waking : and brings up some thick greenish spit. Her general health has been good, although she has always been a little thin : but she is

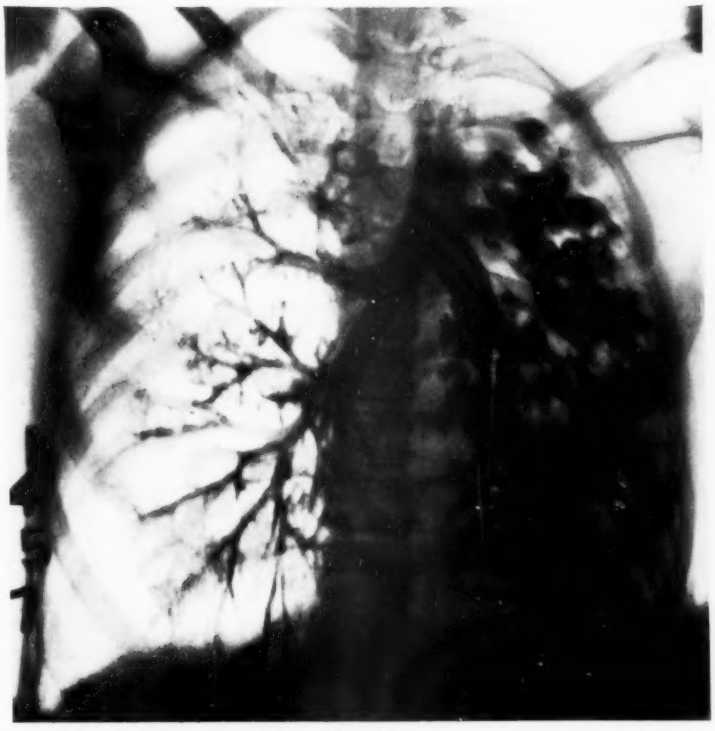


FIG. 2.

full of energy and high spirits, and takes her full share in games. Came under observation, aged 8 years, and has been watched closely until now. The general and local condition has not appreciably changed since then. Obvious physical signs of extensive fibroid change and catarrh in the lower half of the left lung, with flattening and deficient movement on this side : outward displacement of the heart, the apex beat being in mid-axilla in the 5th interspace. Slight cyanosis of the lips, cheeks and fingers, but little or no clubbing of the fingers. Lipiodol-radiograph (Fig 2) confirms the massive fibrosis in the left lower lobe, and shows extensive bronchiectasis of the terminal air tubes on this side, and widening of the main bronchi, displacement of the trachea and heart to the left side. The bronchial tree of the right lung shows normal tapering of its twigs, some of which can be seen passing across the middle line to the left side, indicating that part of the right lung has passed across the mediastinum.

Commentary. A case of extensive unilateral bronchiectasis, with massive fibrosis of the left lung, and displacement of mediastinal structures : following measles and pneumonia. General health fairly good. Duration, 11 years.

In our last paper particular stress was laid upon one feature of the pathological process in acute broncho-pneumonia. That feature was the presence, and often great severity, of acute interstitial inflammation of the bronchial walls, alveolar septa and general stroma of the lungs. It was pointed out that this condition favours a prolonged persistence of the inflammation, hinders rapid and perfect resolution, and in a proportion of cases brings about chronic pathological changes in the lungs. Two of the most important of these chronic changes, bronchiectasis and fibrosis of the lungs, are the subject of the present study. These two conditions are intimately bound up one with the other and cannot be considered entirely apart.

Bronchiectasis.

Acute bronchiectasis. A very common post-mortem finding in the lungs of children who die of acute broncho-pneumonia is widening of the lumina of small bronchi, especially those in the centres of consolidated patches. The term acute bronchiectasis or bronchiolectasis is frequently used to designate this. But there are two entirely distinct types of change which may produce this widening of the tubes. In severe cases of broncho-pneumonia it is sometimes due to a destructive change in the walls of the bronchi (ulcerative bronchitis) which is described in detail below, and which, in the event of the patient's survival, necessarily leads to permanent changes in the lungs. In many cases, however, the widening of the bronchial lumen is due to pure dilatation, with acute overstretching of the wall, unaccompanied by any important structural change. This latter condition, very common in acute broncho-pneumonia, affects small bronchi in the consolidated areas and also those in unconsolidated parts. It is analogous to acute emphysema of the alveoli, which often accompanies it: it is probably due to the same causes, and is doubtless capable of complete recovery without permanent damage. It is probably this condition which Rilliet and Barthez[8] described as 'acute bronchial dilatation' occurring occasionally in acute broncho-pneumonia.

In descriptions of acute bronchiectasis it is not always clear which of these two entirely different conditions is intended; and indeed, without microscopic examination, it may not be possible to distinguish them. In order to avoid confusion it seems advisable to restrict the application of the term acute bronchiectasis or bronchiolectasis (for it is almost exclusively the small tubes which show the change) to the condition of true dilatation.

It is not, however, with acute bronchiectasis that the present study is principally concerned, but with the sequence of changes which, originating in acute respiratory disease, especially broncho-pneumonia, may lead to the development of chronic bronchiectasis.

Chronic bronchiectasis. The mode of development of chronic bronchiectasis is a problem which cannot be said to have been satisfactorily solved. Modern standard text-books of pathology advance various suggestions, none of which seems entirely adequate.

According to Muir[9] 'bronchiectasis may be ascribed to certain mechanical factors acting on a weakened bronchial wall, and . . . fibrosis of the lungs plays a very important part. . . . The chief mechanical factor is forced inspiration, especially that which follows the act of coughing . . . This will be specially effective when the lung beyond is not free to expand . . . as in permanent collapse or in interstitial pneumonia . . . 'The actual contraction of the connective tissue also may play a part, as was maintained by Corrigan.' The association of bronchiectasis with acute respiratory disease in childhood is referred to by Muir, who states that 'it is likely that in many cases of cylindrical bronchiectasis the lesion is started in early life by whooping-cough, the bronchitis of measles or of other diseases . . . In these (cases) the supporting muscular tissue of the bronchi has apparently suffered, though we cannot say why this should be brought about.'

Karsner[10] states that 'the more acute forms of bronchiectasis are due to destructive disease of the wall . . . Such dilatations are due almost entirely to the disease of the wall and not contributed to in any large measure by increased intrabronchial air pressure'. He appears, however, to regard the chronic form as having a different explanation and mentions the factors of weakening of the wall by chronic inflammation, and the dilating effects of cough, accumulation of secretion, and fibrosis of the lung substance between the bronchi.

Kaufmann,[11] who recapitulates the same views, suggests that 'there is a possibility of congenital weakness of the bronchial walls in the bronchiectases of childhood'.

MacCallum[12] favours the view that a partial obstruction of a bronchus, such as can be overcome by the active inspiratory effort, but prevents the egress of air during expiration, leads to 'continuous distension of the obstructed bronchus, which finally widens it and is a prominent cause of the condition known as bronchiectasis'. He admits that 'there are many (cases) where obstruction is not . . . obvious, and these offer difficulties'; and quotes Dr. Crowe as stating 'that in dogs in which he has produced stricture of a bronchus, easily seen through the bronchoscope as an extreme narrowing of the lumen, there is no dilatation of the distal part as long as the bronchus remains uninfected'. He affirms that the only point on which there is agreement is 'that the infection and inflammation which weakens the bronchial wall and destroys its elasticity is a necessary factor.'

It is therefore abundantly clear that agreement has not been reached on the problem of how the cavities are produced, and that, as MacCallum truly states, the question needs further study.

During the course of our study of broncho-pneumonia we met with a series of seven cases in which a succession of changes was traceable which seems to us to throw some light on this problem. The observations recorded in this paper, on which certain conclusions are based, were made during the course of a very full examination of these seven cases, with the help of whole-lung sections. Details of some of the cases are given at the end of the paper.

The first stage of the process which leads to the formation of bronchiectatic cavities was found in a case of prolonged broncho-pneumonia, in which a very severe purulent bronchitis was an outstanding feature and acute interstitial inflammation of the bronchial walls was of more than usually intense degree. At the stage represented by this case the condition of the affected bronchi is as follows :—

The lumen is enlarged and filled with pus; the epithelial lining is completely destroyed; all trace of muscle in the wall has vanished; in some instances every vestige of the original wall, including the cartilage, has disappeared and the bronchus is represented by a space bounded directly by consolidated alveoli (Fig. 9). Bronchi may be found whose walls are in process of being destroyed. Sometimes only a part of the wall is affected (Fig. 10). At one side of the bronchus it may be intact while at the

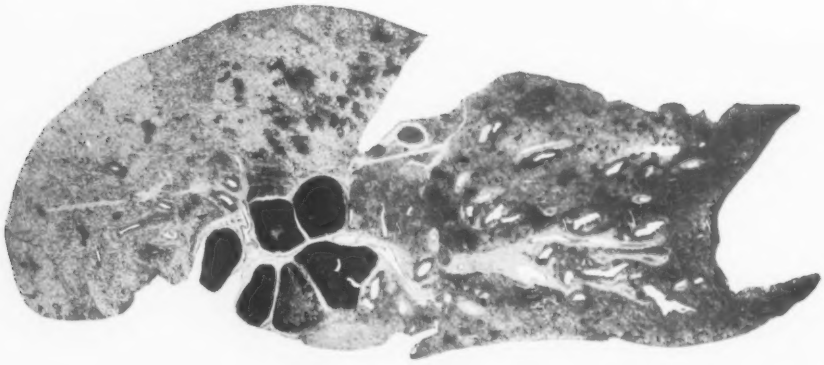


Fig. 4.

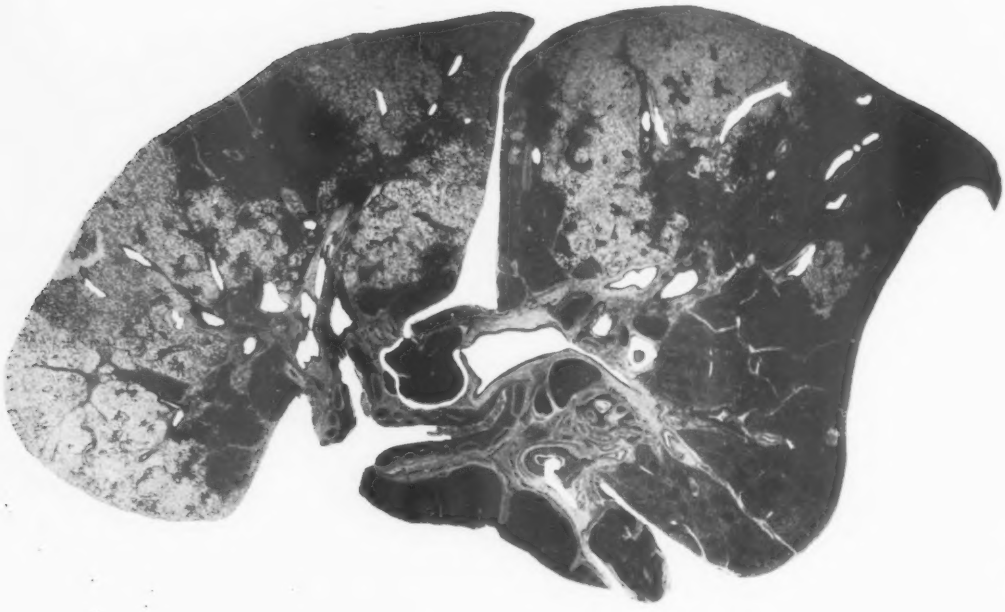
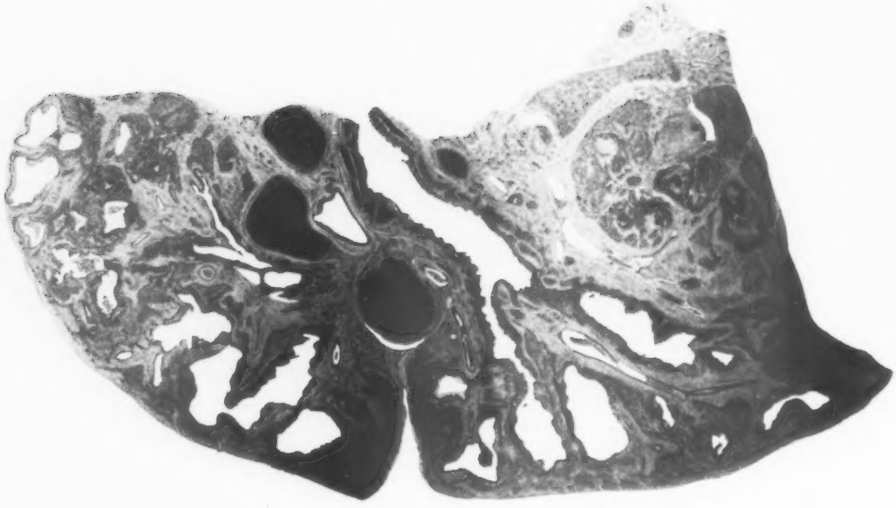


Fig. 3.



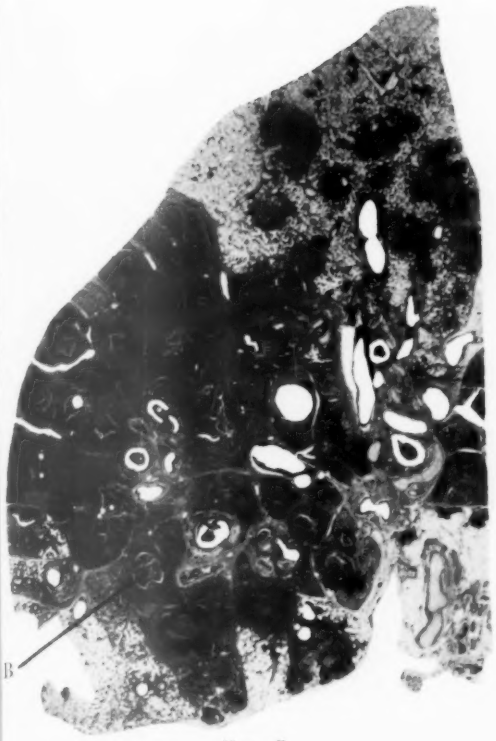


FIG. 5.

FIG. 6.

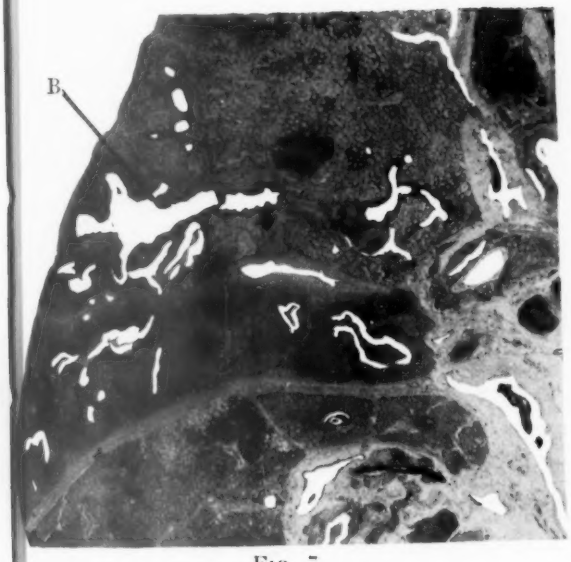


FIG. 7

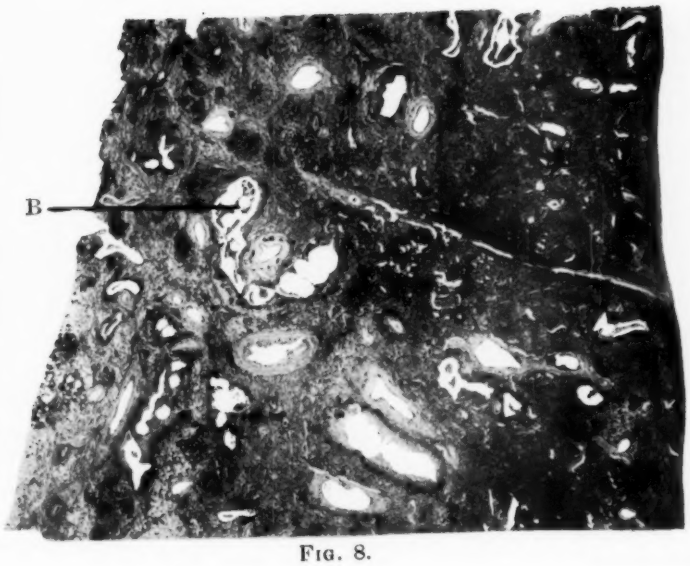


FIG. 8.

(*For Description of Figures, see page* 189).

Fig. 9.

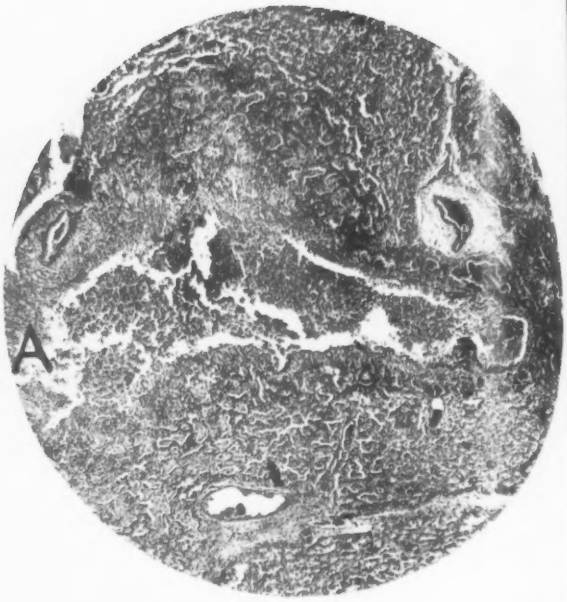


Fig. 10.

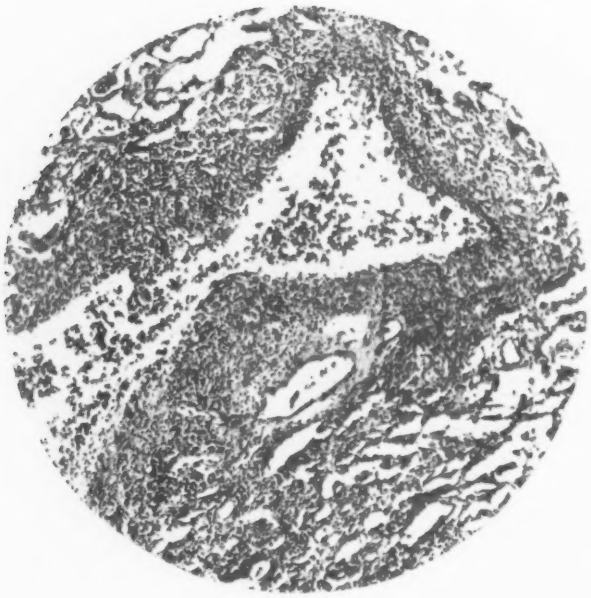


Fig. 11.

Fig. 12.

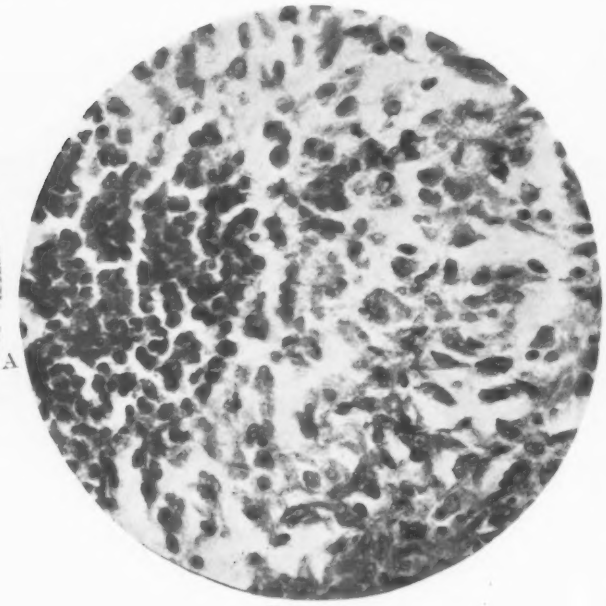


Fig. 13.

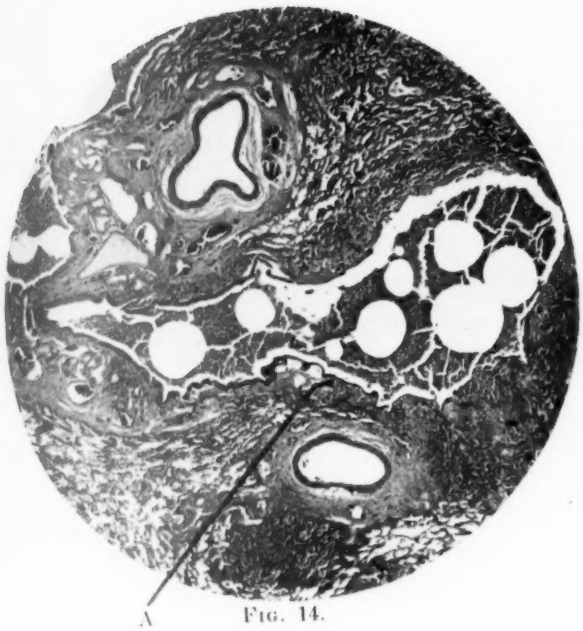


FIG. 14.

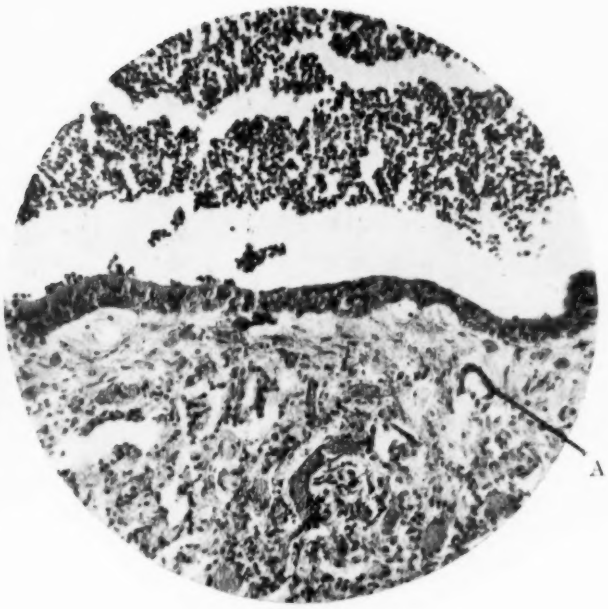


FIG. 15.

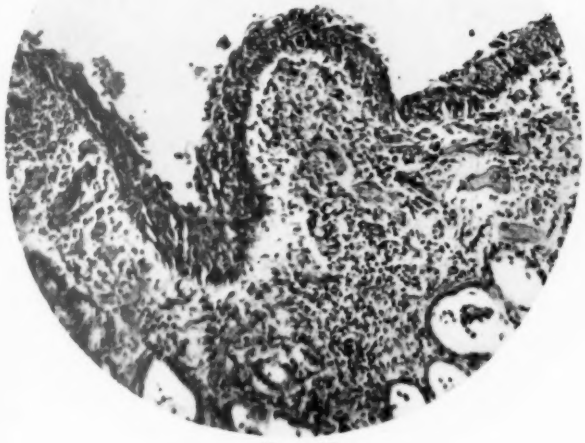


FIG. 16.

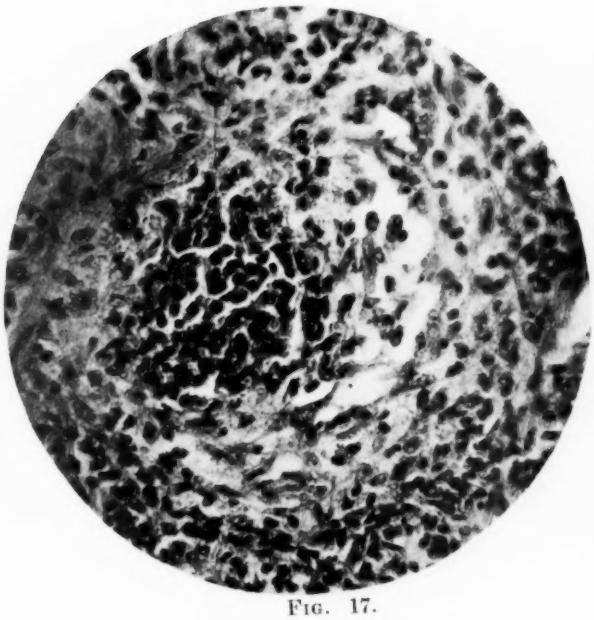


FIG. 17.

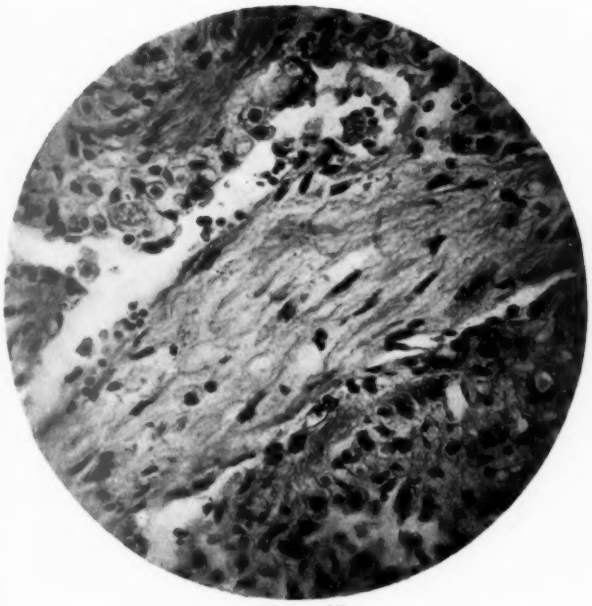


FIG. 18.

FIG. 19.

other it is necrotic or has disappeared. The process of necrosis and suppuration which destroys the bronchus wall may involve adjacent alveolar tissue to a variable extent, or may be confined to the bronchus. In some instances the great enlargement of the lumen at the part where the wall is destroyed makes it obvious that a certain amount of alveolar tissue also has perished. In this way there are formed cylindrical or saccular expansions of the bronchi, which are clearly not due to dilatation properly so called, but to a process of excavation, with loss of tissue from the bronchus wall and sometimes also from the surrounding lung substance, as a result of necrosis accompanying suppuration (Fig. 5 or 6). The cavities are often very sharply defined. This is the destructive change in the wall to which Karsner ascribes ' the more acute forms of bronchiectasis '. We suggest that, at least in certain cases, it is responsible for the development of the chronic form also, and is the fundamental change underlying that condition.

At a slightly later stage (represented by Case II) the early beginnings of repair are apparent. The cavities heal by granulation. From the wall of the cavity (usually formed at first by consolidated alveoli) there springs a growth of young fibroblasts and capillaries which forms a granulation-tissue membrane around the space. Fig. 12 and 13 show the earliest stage of this healing process at one side of a bronchus whose wall has been completely destroyed.

The growth of this granulation tissue continues until a definite fibrous layer, at first extremely vascular, bounds the cavity. After a time epithelium, surviving in neighbouring parts of the bronchus which have not suffered destruction, grows over the surface of the new granulation-tissue wall and gives the cavity an epithelial lining continuous with that of the bronchus. This relining process begins even while there is ample evidence of the persistence of active inflammation. Healing of the cavities in this way is represented at various stages, in Cases I, IV and V in our series. It is illustrated in Fig. 11, 14 and 15. The bronchus wall shown in Fig. 14 has remained intact at one side, while destruction at the other side has produced a saccular expansion of the lumen. The destroyed part has been replaced by a new wall composed of young and very vascular fibrous tissue, among which no trace of muscle or cartilage is to be found (Fig. 15). Over a part of this new wall a layer of epithelial cells has spread, the covering being not yet quite complete. The epithelium is of a cubical type and not ciliated.

The beginning of fibrosis of the lung substance between the ectatic bronchi may be found at this stage, but is only of slight degree. In our cases it was confined to alveoli immediately related to affected bronchi, and took the form of proliferation of fibroblasts in the alveolar walls which caused considerable thickening, and in two cases an exudate in the alveolar spaces was in process of organization by means of leashes of young fibroblasts and capillaries which sprang from adjacent alveolar septa (Fig. 18). Nowhere, at this stage, was dense contracting fibrous tissue found ; nor were fibrous pleural adhesions present.

Later on the granulation-tissue wall of the cavity becomes thicker and more definitely fibrous. There is no regeneration of muscle or cartilage, and little or no new elastic tissue appears to be formed. The new wall may be as thick as, or thicker than, the original one, and may have a complete epithelial lining, but it is a purely fibrous structure, lacking in all those elements which endow the normal bronchial wall with strength and elasticity (Fig. 16).

The absence of muscle, cartilage and elastic tissue, and loss of characteristic structure in the walls of ectatic bronchi have been repeatedly described. This change is usually ascribed to 'atrophy' of these essential elements as a result of chronic inflammation or strain. To our mind, the fibrous membrane which lines these cavities is often not the original wall at all, but a new structure formed from granulation tissue around a space produced by an active process of destruction.

The true chronic stage of bronchiectasis is represented in our series by Cases VI and VII. In Case VI (Fig. 4) the amount of bronchial dilatation was not very great. In the lower lobe some of the bronchi showed a cylindrical expansion of the lumen but there were no large cavities. The walls of these bronchi presented exactly the changes which have been described. One is illustrated in Fig. 16. This wall is composed of a considerable thickness of vascular fibrous tissue covered with epithelium; muscle and cartilage are absent. Case VII (Fig. 3) was one of typical, very severe chronic bronchiectasis. The whole left lung was occupied by cavities of various sizes, mostly large. In the walls of the cavities there was no muscle, no cartilage, virtually no elastic tissue. Most of them had an epithelial lining, the cells being of a small debased cubical type.

At this stage the lung substance between the cavities shows advanced chronic interstitial pneumonia, being occupied by dense fibrous tissue, among which may be detected the remains of obliterated alveoli and small bronchi. This was the state of affairs in both of our chronic cases. In Case VII ,dense fibrous pleural adhesions were present. The condition of the lung substance in the lower lobe of Case VI is shown in Fig. 19. The part illustrated is typical of practically the whole lobe. Yet there was no evidence that the contraction of this very dense fibrous tissue had stretched the bronchial walls. On the contrary, it seemed rather to have had the opposite effect, for in places the walls of the dilated bronchi were thrown into folds, showing that they were certainly not expanded to their full capacity. This is illustrated in Fig. 16.

In Case VII (Fig. 3), the cavities were so numerous and of such a size that the lung substance between them was represented by little more than broad fibrous septa, in some of which remains of alveoli, more or less completely obliterated, were demonstrable. The smaller bronchi in communication with those from which the cavities were formed, had also suffered obliteration.

From the observations which have been recorded the following conclusions have been drawn, offering an explanation of those cases of chronic bronchiectasis

which follow acute respiratory diseases in children, especially broncho-pneumonia. The initial change which underlies the whole process occurs during the acute phase of the disease, and takes the form of severe acute interstitial inflammation of the bronchial wall, going on to necrosis and suppuration. This causes the formation of a cavity by loss of tissue from the bronchus wall, and excavation of a certain amount of adjacent alveolar substance in most instances. The cavity may be cylindrical or saccular in shape according to the extent of the excavation and whether it affects the whole circumference of the bronchus equally or is more extensive at one side. Subsequently the cavity is lined by granulation tissue, becoming fibrous, and finally may be covered by bronchial epithelium, usually of a modified type. Thus a new wall is constituted round a bronchial lumen which has been enlarged to a greater or less degree according to the extent of the initial destructive process.

According to this view, a bronchiectatic cavity is not a dilated bronchus, but an excavation in the lung substance, starting in a bronchus, and is strictly analogous to a tuberculous vomica. It is not necessary, in order to explain the existence of the cavities, to postulate the operation of any of the factors usually credited with dilating effects. Destruction of tissue, and not dilatation, is the essence of the process. Nevertheless those factors may be instrumental in enlarging the cavities after they are formed. It may readily be assumed that anything which might tend to dilate a bronchus would be doubly effective in stretching the relatively weak fibrous walls of the cavities. Secretion and inflammatory products are bound to accumulate in the cavities, especially as the absence of muscle and ciliated epithelium deprives the altered bronchi of the principal means by which a healthy bronchus rids itself of secretion. This accumulation makes probable the occurrence of that partial obstruction to which MacCallum attaches importance as a dilating factor. Infection flourishes in the stagnant contents and causes enlargement of the cavities by further ulceration and excavation. Fibrosis of the lung substance, especially close to bronchi, accompanies the process of healing of the cavities and is probably constant in chronic cases. It may, in some instances, by contraction tend to dilate the cavities further, as Corrigan believed, but this can be only after the bronchiectasis is well established, and we have found no direct evidence that it has this effect.

In putting forward this view of the mode of formation of bronchiectatic cavities, we do not claim that it explains all cases. Our studies have been confined to cases in children, in whom the disease could be clearly traced to its origin in broncho-pneumonia. Certain cases which develop without any evidence of antecedent acute respiratory disease may demand some other explanation. We are, however, of opinion that very many cases of chronic bronchiectasis (many even of those which manifest themselves only in adult life) owe their origin to broncho-pneumonia or bronchitis in childhood; and there is a considerable body of evidence to support this view. Where bronchiectasis is due to foreign bodies in the lungs, the presence of infection is probably an essential factor, and the process by which the cavities are formed may well be similar to that which we have described. We have not, however, any observations of our own to record with regard to this.

Pathology of Fibrosis of the Lungs.

Non-tuberculous chronic fibrosis of the lungs is usually associated either with gross fibrous thickening of the pleura such as results from long-standing empyema, or with chronic changes in the bronchial walls, with or without definite bronchiectasis. It is with the latter type that the present study is concerned.

It may be stated that the chronic form of bronchiectasis is always accompanied by some degree of fibrosis of the lungs, but that fibrosis may occur without gross enlargement of bronchial lumen such as could be detected clinically as bronchiectasis. As has been described in the foregoing study, in cases of bronchiectasis where cavities are formed by active destruction, fibrosis of the adjacent lung substance accompanies the process of reconstruction of the wall of the cavities. It begins in the immediate vicinity of the damaged bronchi, but may ultimately lead to an almost complete fibrous replacement of the alveolar tissue throughout the affected portion of the lung. The fibrosis is brought about in various ways.

(*a*) There may be proliferation of fibroblasts, with laying down of new fibrous tissue in the inflamed walls of alveoli adjacent to the damaged bronchi. This leads to great thickening of the alveolar septa and a corresponding reduction in the size of the spaces. Accompanying this change in the wall, there is usually an alteration in the character of the lining epithelium of the alveoli, which becomes cubical instead of flattened, and very much more conspicuous than it ought to be. Fibrous tissue proliferation may affect also the coarse stroma of the lungs, increasing the width of the interlobular septa and the amount of perivascular and peribronchial fibrous tissue. It may be regarded as the result of long continued interstitial inflammation of the lung framework, which in its acute form is so constant a feature of broncho-pneumonia.

(*b*) In certain cases organization of an exudate in the alveolar spaces takes place. The alveoli come to be occupied by strands or leashes of young fibroblasts and their fibres, which pass from alveolus to alveolus, and the origin of which from the alveolar wall at some point may be demonstrable. This remarkable appearance is illustrated in Fig. 18, which shows the process at an early stage. Its end result, if the patient survive, must be obliteration of the alveolar spaces by fibrous tissue and massive fibrosis of the affected part. This is what is known as 'organizing pneumonia.' Sometimes it occurs throughout a large area of lung as a direct result of pneumonia in which the exudate does not resolve, but becomes organized. During the course of our present investigation, we have seen two cases of this kind, in neither of which was any bronchial dilatation present. The same process, but limited to alveoli adjacent to the damaged bronchi, was observed in Case IV of our bronchiectasis series, in which it contributed materially to the early fibrosis of the lungs noted in those cases. At a later stage, when many alveolar spaces have been obliterated and the new fibrous tissue has become dense, it would be difficult, if not impossible, to distinguish fibrosis due to this process from that produced in other ways.

(*c*) In bronchiectatic lungs, many small bronchi communicating with those from which the cavities are formed become obliterated. We were able to observe the process of obliteration at various stages in our series of cases. During the initial stage of ulcerative bronchitis, the smaller bronchi may suffer in exactly the same way as the larger, and have their walls completely destroyed. The healing process which follows, with growth of granulation tissue forming a new wall around the cavities may, in the case of small bronchi, lead to obliteration, the whole lumen being filled with proliferating fibroblasts and new capillaries. An example of this obliterative bronchiolitis, taken from Case II, is shown in Fig. 15. In this way many small bronchi may be completely obliterated. In some instances the new granulation tissue does not occupy quite the whole lumen; spaces are left which may ultimately be lined with bronchial epithelium. This produces the curious effect of a bronchus divided into a number of minute epithelial-lined spaces separated by masses of fibrous tissue. This obliterative bronchiolitis contributes to fibrosis of the lungs not only by the formation of fibrous tissue in the small bronchi themselves, but also by producing in the alveoli communicating with them a permanent condition of collapse, which must result in further fibrosis.

In conclusion it may be stated that the pathological processes underlying bronchiectasis and pulmonary fibrosis are intimately connected. Destructive changes in the bronchial walls, the processes of healing which follow these, and the persistence of infection in and around the damaged bronchi, are together responsible for the fibrosis which accompanies bronchiectasis. Apart from those cases where fibrosis is of pleural origin, and occasional rare cases of organizing pneumonia, it would seem doubtful whether massive fibrosis of the lungs takes place in the absence of severe bronchial damage, although it is evident that the degree of bronchial damage need not be such as to produce bronchiectasis clinically obvious. Case VI of our series (Fig. 4) is an instructive example of this, where, with massive fibrosis of a lobe, only very slight bronchial dilatation was present. Yet the bronchial walls were profoundly altered, and the pathological changes which they showed were precisely the same as those in Case VII (Fig. 3) except in respect of the size of the cavities. For this reason cases of frank bronchiectasis, and cases of fibrosis of the lungs without obvious bronchiectasis (if not of pleural origin), may be reasonably regarded as belonging to the same pathological group; and the extended use of lipiodol in radiography of the chest will probably reveal bronchial enlargement in many cases of 'fibroid lung' previously believed to be free from bronchiectasis.

Abstracts of Fatal Cases.

(The case numbers are those used in the "Pathological Study").

Case I. Broncho-pneumonia of seven weeks' duration, with ulcerative bronchitis. (Fig. 5, 9 and 10).

Male, aged 6 months. Eighth child. Four others had died in infancy, 2 shortly after birth and 2 of broncho-pneumonia following measles and whooping-cough. House of 2 small rooms, with leaking roof. Breast-fed for 2 months and thereafter on cow's milk under direction of child welfare clinic. Turned ill 2 days before admission in February, 1926, with fever, heavy

breathing and cough. Died 7 weeks after admission. While under observation, there was a remittent temperature, a steady loss of flesh, a troublesome cough, considerable dyspnœa, generalized bronchitis, and, after about a week, evidence of consolidation in the right upper lobe, followed by consolidation in both lower lobes.

Post-mortem examination. Body very emaciated. Much purulent secretion in main air-passages. Pleural sacs healthy. Right lung—anterior portions of upper and lower lobes and most of middle lobe very emphysematous (vesicular and interstitial); posterior part of upper lobe, most of lower lobe, and middle lobe near root consolidated as a result of patchy pneumonia and collapse; bronchi greatly inflamed, filled with pus, and slightly dilated. Left lung—whole upper lobe and anterior part of lower lobe emphysematous; posterior portion of lower consolidated; bronchi as above but not so severely affected. Mediastinal glands much enlarged. Heart and other organs atrophied. Little or no obvious toxic change.

Microscopic examination. In general the condition is one of purulent bronchitis with both discrete patches and extensive areas of confluent broncho-pneumonia. Changes are most advanced in the right upper lobe, where clinically consolidation was first noted. Here the bronchitis has been intense and the walls have undergone complete disintegration, with very considerable erosion and excavation. In this case the process of destruction was still active at the time of death, unchecked by any effort at repair.

Case II. Broncho-pneumonia of several weeks' duration, following measles, with severe bronchial damage. (Fig. 6, 12, 13 and 17.)

Female, aged 2 years. This case was reported (Case VI, p. 123) and illustrated (Fig. 11) in the third paper of this series[13], but it is thought desirable to amplify the description of the bronchial changes. These are widespread and are most advanced in the smaller bronchi. All the latter are plugged with thick pus, and show some degree of distension or excavation; in some, no vestige of the original wall remains and the lumen is surrounded merely by consolidated alveolar tissue. While the inflammatory process was thus intensely active at the time of death, in a few instances there has been an attempt at repair. Here and there in the walls of the cavities, very young granulation tissue is visible and a beginning has been made of the reconstitution of the wall. Efforts at repair are also seen in several of the capillary bronchioles, and here the effect has been different; organization is leading to obliteration. These bronchioles are represented by small circular patches of fibro blasts and delicate connective tissue fibrils surrounding a clump of degenerated polymorphonuclear cells. There is therefore an obliterative bronchiolitis in progress.

Case IV. Broncho-pneumonia of nine weeks' duration, with early bronchiectasis. (Fig. 7 and 11.)

Female, aged 15 months. Four other children, one in hospital with tuberculosis. Breast-fed for 11 months. First tooth at 7 months. No previous illness, but for 2 weeks before admission had a cough. Admitted in September, 1926, at age of 12 months, having been acutely ill with fever, cough and grunting breathing for 24 hours. Diagnosed as severe acute bronchitis, possibly broncho-pneumonia. Marked constitutional disturbance but no definite consolidation. After a week, improvement occurred and temperature came down by lysis. On 14th day, temperature rose to 101·4° and a rash developed. Scarlet fever suspected but not confirmed at the fever hospital, child being sent home after 3 days. Progress at home unsatisfactory; continued to cough; appetite poor; no energy or inclination to move about; weight lost. Re-admitted in November, 8 weeks after the onset of the acute respiratory illness. No rise of temperature, but child pale and listless. Weight 12½ lb. "Chesty" cough. Moist sounds in both lungs, with a suspicion of dulness at the left base. Four days after admission, temperature rose for first time to 101°; pulse uncountable; respiration 56. Unpleasant odour noticed in neighbourhood of patient at this date. Fifteen c.c. of thick foul-smelling pus removed through 9th left interspace. Death occurred 5 days after admission. Whole illness lasted therefore for about 9 weeks.

Post-mortem examination. Body that of a small and poorly nourished child. About 1 oz. of thick yellow pus with a very foul odour in left pleural sac, with much fibrino-purulent exudate in relation to it. Right pleura healthy. Left lung—mixture of collapse and patchy pneumonia; numerous bronchiectatic cavities with a smooth greenish lining in lower lobe. Right lung—more

extensively consolidated, again in a patchy fashion; innumerable small bronchiectatic cavities with a yellowish lining membrane in pneumonic areas. Mediastinal glands much enlarged. Heart atrophied. No toxic changes in spleen, but liver fatty.

Microscopic examination. There is some discrete broncho-pneumonia in the upper and more extensive consolidation in the other lobes. The bronchi are all pathological, but those in the apical regions show overstretching rather than serious destructive change. Bronchiectatic cavities are most numerous in the lower lobes and some are of considerable size. There the bronchial inflammation has been of great severity. In many cases, the original wall has completely disappeared; in others, part of the circumference is more or less intact, while the remainder is destroyed. The process is still active, but in all there has been some attempt at repair and reconstitution of the wall by granulation tissue. There is early fibrosis of the lung in the affected parts; alveolar walls are thickened and very cellular; in places the lining alveolar cells tend to be cubical; there is broadening of the septa.

Case V. Early chronic bronchiectasis, with terminal acute broncho-pneumonia. (Fig. 8, 14 and 15.)

Female, aged 16 months. Indefinite history of epilepsy on the mother's side. One other child, aged 12, healthy. Artificially fed from birth. Cut first tooth just before admission. Mentally defective. Had had one severe and numerous minor fits. Several indefinite illnesses, some of which were evidently respiratory. Admitted in February, 1926, having been ill for 4 days with gastro-intestinal symptoms, cough and grunting respiration. Ill-nourished but not obviously rachitic. All the signs of early broncho-pneumonia on admission. Died 11 days later, consolidation having become progressively more marked in both lungs.

Post-mortem examination. Right pleural sac moist. Some loose fibrous adhesions over left lung. Extensive consolidation along posterior borders of both lungs. Consolidated parts dark red on section, with yellow mottling round bronchi. Mediastinal glands greatly swollen. Heart not greatly altered. Little toxic change in organs.

Microscopic examination. Chief interest centres in the condition of the bronchi in the right lung. They are all acutely inflamed but many show in addition changes of a more chronic nature. In general, there is quite considerable dilatation. In the more dilated of the larger bronchi, in which the chronic changes can be studied best, there is profound alteration of the walls. The epithelium may be entirely absent or modified to a low cubical type. The sub-epithelial tissue is greatly increased in amount, and appears as very vascular granulation tissue thickly infiltrated with polymorphonuclear cells. In some instances practically the whole thickness of the wall is composed of tissue of this type, muscular structure being unrecognizable. Some of the large bronchi near the root show these changes only in certain parts of their walls, while other parts appear almost healthy. The picture is one of recent acute inflammation arising in bronchi which were previously the seat of chronic changes associated with bronchiectasis. In the lung substance itself, there is no general fibrosis, but there are areas, closely related to diseased bronchi, where there is diffuse overgrowth of connective tissue varying from slight increase in the thickness of the alveolar walls to the production of a structure resembling granulation rather than lung tissue. Careful examination reveals that the fibrosis is in large part the result of organization of an exudate in the alveolar spaces.

Case VI. Chronic fibrosis of the lung, with slight bronchiectasis; terminal acute broncho-pneumonia. (Fig. 4, 16 and 19.)

Female, aged 6 years. Mother died in childbirth 6 months before patient's fatal illness. Five other children alive; 2 died in infancy. Home conditions bad. Past history unreliable. Said to have been always delicate and subject to bronchitis, and about a year before admission to have suffered from a respiratory illness, the details of which were not known. Was "always coughing." Admitted in March, 1926, having been taken suddenly ill about 30 hours previously. Was fevered and had vomited repeatedly. On admission, temperature 104·8°; pulse 160; respiration 32. Semi-comatose and toxic. Throat inflamed; swab negative for diphtheria. Cerebro-spinal fluid normal. Blood culture sterile. Leucocytes 6,200. Death occurred 7 days after admission. Two days before death, the lungs "showed signs of broncho-pneumonia."

Post-mortem examination. Large quantity of turbid fluid in left pleura, with masses of thick loosely-attached fibrin on serous surface. Right pleural sac healthy. Left lung—acute broncho-pneumonia in upper lobe; slight dilatation of bronchi and fibrosis, in addition to pneumonia

with areas of suppuration, in lower lobe. Right lung—commencing broncho-pneumonia, with purulent bronchitis and some bronchial dilatation. Marked enlargement of mediastinal glands. Early fatty change in liver and kidneys.

Microscopic examination of left lung. The lymphatic vessels at the root are greatly dilated and full of pus. The upper lobe is in great part air-containing, but shows bronchitis and small patches of broncho-pneumonia. The lower lobe similarly shows evidence of acute inflammation, with suppuration in several places, but there are also very striking chronic changes. The size of the lobe is below normal, owing partly to collapse consequent on pleural effusion and partly to fibrosis. The larger bronchi are dilated, but there are no big bronchiectatic cavities. Their walls are much altered. In most an epithelial lining is present, but seldom of normal character. Muscle fibres are hardly discernible; the walls are composed of very vascular granulation tissue, densely infiltrated with lymphoid and other mononuclear cells. In some instances, the appearance of reduced alveolar spaces lined with cuboidal cells among this tissue shows that most of the original bronchus wall has been destroyed. A striking feature is the lymphocytic infiltration of peribronchial tissue.

The smaller bronchi are not dilated; many indeed are reduced in size. Each is surrounded by a dense collection of small mononuclear cells. In some places no true lumen can be distinguished, but, in the midst of vascular connective tissue and lymphocytes, merely a few small spaces lined by low columnar epithelium. In addition to these widespread chronic bronchial changes there is very extensive fibrosis in this lobe, which would appear to have resulted both from the obliteration of bronchi and from proliferative changes in alveolar walls; organization of exudate in alveolar spaces is not demonstrable. What little lung tissue in this lobe is not affected by interstitial pneumonia is collapsed.

Case VII. Advanced unilateral bronchiectasis, with terminal acute broncho-pneumonia. (Fig. 3).

Male, aged 6 years. Fairly healthy in infancy, though rather late in cutting teeth and walking. Subject to "eczema" from an early age. Measles at 2 years; no complication. Admitted to Royal Infirmary, Edinburgh, in October, 1927, at age of 4½ years for treatment of infantile dermatitis. Ten days later developed pneumonia, which dragged on for many months and passed directly into a condition of bronchiectasis. Was in hospital for more than 8 months on end and was treated latterly by repeated bronchoscopic lavage. First admitted to the R.H.S.C. in July, 1928, i.e., 10 months after the onset of the respiratory illness. At that date, was coughing up two or three cupfuls of thick offensive sputum each day. General development quite good, but nutrition poor. Fingers clubbed. Physical signs confined to left lung. Mediastinal structures slightly drawn over to left side. Remained in hospital till January, 1929, i.e. for 6 months. On discharge, was coughing up ½ to 3 ozs. of pus each morning. Re-admitted in February, 1929, having been fairly well in interval and having gained 2 lb. Began to have a slight evening rise of temperature and on tenth day to have all the signs of acute broncho-pneumonia. Died 14 days after re-admission, i.e. about 18 months after the onset of the original pneumonia.

Post-mortem examination. Left pleural sac completely obliterated by dense fibrous adhesions. Right pleura acutely inflamed. Left lung smaller than right and occupied throughout by a large number of bronchiectatic cavities, the walls of which were fairly smooth and of a deep red colour, and the contents of which consisted of very foul pus. Cavities separated by septa of completely fibrosed lung substance. Right lung voluminous and the seat of widespread acute broncho-pneumonia. No chronic changes. Tracheo-bronchial and broncho-pulmonary glands enormously enlarged. Heart dilated and right ventricle possibly slightly hypertrophied.

Microscopic examination of left lung. Most of the cavities have an incomplete lining of small epithelial cells, beneath which is a layer of vascular connective tissue thickly infiltrated with lymphocytes. This layer varies greatly in thickness and in places its free edge is necrotic. It merges into denser fibrous tissue, amongst which are to be found alveolar spaces lined by altered epithelium and small bronchi more or less completely obliterated. The whole of the septa between the cavities is composed of this fibrosed and obliterated lung substance. The medial part of the lower lobe shows extensive fibrosis without cavities. The absence of bronchi of any size in this area, and the presence (where bronchi apparently ought to be) of small spaces lined

by cubical epithelium, surrounded by aggregations of lymphocytes, suggests that obliterative bronchitis was a marked feature of the process in this part of the lung. Cartilage is present only in the main bronchus. Elastic tissue can be demonstrated by special staining in the walls of the blood vessels, in the main bronchus, and in the walls of such alveoli as remain, but is completely absent in the walls of the cavities.

Summary.

1. A brief historical survey of bronchiectasis and fibrosis of the lung in childhood is given, followed by clinical records of two cases.

2. The genesis of these two conditions is traced in a series of seven fatal cases.

3. The conclusion is reached that many cases have an origin in an acute respiratory illness.

4. Bronchiectasis ensues when inflammation is of such severity as to disorganize the bronchial wall. The cavities so formed are subsequently lined by a new wall of granulation tissue.

5. Fibrosis of the lung necessarily accompanies established bronchiectasis.

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DESCRIPTIONS OF FIGURES.

Fig. 1. Lipiodol-radiogram of Clinical Case A.
Fig. 2. Lipiodol-radiogram of Clinical Case B.
Fig. 3. (Case VII. Male, aged 6 years). Advanced unilateral bronchiectasis in left lung. Acute broncho-pneumonia in right lung. Great enlargement of root glands.
Fig. 4. (Case VI. Female, aged 6 years.) Chronic fibrosis, with slight bronchiectasis, in lower lobe of left lung. Marked glandular enlargement.
Fig. 5 (×2.) (Case I. Male, aged 6 months.) Ulcerative bronchitis and confluent broncho-pneumonia in right upper lobe. Bronchi distinctly enlarged; majority filled with pus. B= bronchus illustrated in Fig. 7.
Fig. 6 (×2½.) (Case II. Female, aged 2 years.) Ulcerative bronchitis and acute broncho-pneumonia in right upper lobe. Plugs of pus in excavated bronchi. Considerable collapse between pneumonic patches.
Fig. 7 (×2½.) (Case IV. Female, aged 15 months.) Early bronchiectasis in right lung. One cavity of considerable size towards pleural surface. Several other bronchi enlarged. Confluent broncho-pneumonia in relation to affected bronchi. Obliteration of interlobar fissure. B= portion of bronchiectactic cavity illustrated in Fig. 9.
Fig. 8 (×2.). (Case V. Female, aged 16 months.) Early chronic bronchiectasis with termiral acute pneumonia in left lung. B = bronchus illustrated in Figs. 12 and 13.
Fig. 9(×60.) (Same case as Fig. 3). Ulcerative bronchitis. Bronchial wall completely destroyed and margin of cavity formed by consolidated alveoli. Plug of pus in lumen.
Fig. 10(×60.) (Same case as Figs. 3 and 7). Ulcerative bronchitis. Bronchial wall completely destroyed at one side (A) and relatively healthy at the other.
Fig. 11(×110.) (Same case as Fig. 5). Early bronchiectasis. Diverticulum of large cavity. Reconstitution of wall by granulation tissue.
Fig. 12 (×110.) (Case II.) Ulcerative bronchitis with beginning of healing. A= young granulation tissue.
Fig. 13 (×300.) Magnification of area A in previous photograph. Young fibroblasts sprouting out and replacing acute inflammatory products. Clump of polymorphonuclear cells to left of field.
Fig. 14 (×60.) (Same case as Fig. 6). Bronchus in which disintegration and erosion of half of the circumference had occurred and in which repair was in process. Intact wall on the left; denuded and excavated wall on the right of the field. A = portion of wall shown in Fig. 13.
Fig. 15 (×120.) Magnification of above. Vascular granulation tissue in wall, in which a few modified alveolar spaces (A) are visible. Extension of epithelium to form a new lining for eroded portion. New epithelial cells, seen on right, of a lower grade than original epithelium. Purulent exudate in lumen.
Fig. 16 (×120). (Same case as Fig. 2). Wall of damaged, slightly dilated, bronchus. Whole thickness of wall composed of very vascular fibrous tissue, infiltrated with inflammatory cells; muscle absent. Epithelial lining formed of several layers of small cuboidal cells.
Fig. 17 (×300.) (Same case as Fig. 4). Obliterative bronchiolitis. Original wall of bronchus destroyed. Organization of exudate in lumen by young fibroblasts in process and leading to obliteration. Small amount of pus still present in centre.
Fig. 18 (×300.) (Same case as Figs. 6, 12 and 13). Organizing pneumonia. Alveolar space seen, partly occupied by a mass of proliferating fibroblasts and young connective tissue fibres attached to the wall at one point. A few inflammatory cells, remnants of exudate, present.
Fig. 19 (×120.) (Same case as Figs. 2 and 14). Chronic fibrosis of lung, with obliteration of alveoli. A few remnants of alveloi represented by small epithelial lined spaces. Dense aggregation of lymphocytes marks site of obliterated bronchus.

ARACHNODACTYLY.

BY

MAURICE L. YOUNG, M.D., M.R.C.P.

The first description of arachnodactyly dates back to 1896.

In that year Marfan[9] showed a case of a child exhibiting unusual length and slenderness of the bones of feet and hands, and pointed out that other abnormalities coexisted; he suggested the term 'Pieds d'araigne' (Spider feet) but decided upon that of 'Dolicho-stenomélie'; the possibility of endocrine disorder was first recognized by him, but he was unable to substantiate his theory. Six years later Marfan's case was shown by Méry and Babonneix[10] who showed by means of skiagrams that some activity of epiphyseal cartilages was present, and used the term 'Hyperchondroplasia'; they also mentioned syphilis as a possible factor. In the same year (1902) Achard[1], using the term 'arachnodactyly' for the first time, demonstrated the condition in a girl aged 18 years, where both familial and hereditary influences were marked. In the following year Poynton[15] showed a case to the Medical Society of London under the heading of 'Atavism,' which seems without doubt to have been one of arachnodactyly. On this occasion a member present at the meeting suggested that the condition might belong to the group of muscular dystrophies. In 1914 Borger[2] described two cases in Germany, and laid stress upon its likeness to acromegaly. Salle[21] in the same year spoke of a combination of giant growth and arachnodactyly. Thursfield[24] in 1917 favoured the dystrophic view. He drew attention to the atony and ill-development of the entire musculature of body and limbs, and laid stress upon its resemblance to amyotonia congenita. In the same year Rietschel[18] described a case in which the orbital fissures were obliquely placed, and therefore likened the condition to mongolism. Poynton and Maurice[16] in 1913 demonstrated an instance in which the onset was believed to start in later life, at the age of 6 years; they favoured the endocrine rather than the dystrophic theory. In 1924 Ormond and Williams[12] quoted the details of a case with special reference to ocular symptoms. The first case to be described in America was that by Piper and Irvin-Jones[13] who regarded congenital heart disease as a prominent feature of arachnodactyly, and described the post-mortem appearances of a case in which this was present. Schlack[22]in 1926 recorded the only instance with symptoms which suggested definite pathological changes in the nervous system.

From a review of the literature it seems evident that the condition is a definite clinical entity, and although various theories of the causation have been suggested no one of them is universally accepted.

Only twenty-two cases appear to be on record. Four cases are described in this paper. One is an undoubted instance of amyotonia congenita; in another the atonicity of the musculature is less striking but evident. The remaining two cases are, I think, unique in that they are brother and sister. Their mother was a similar instance of arachnodactyly, and moreover all three members of this family showed many other striking congenital abnormalities.

Ætiology.

Various theories of the causation of this condition have been mentioned above. These may be conveniently examined under their separate headings.

(*a*) *An endocrine disorder.*

Consideration of recorded cases and those of my series shows that with perhaps two exceptions the onset of arachnodactyly takes place during intra-

uterine life. Of 26 cases, in 16 the condition was noticed at birth. In one (Poynton) it was believed to have started later, and in one of my series (Case 1) it was not noted until some years after birth. In seven cases there is no mention of the date of onset, but of these, six showed obvious congenital abnormalities and the remaining case suggests an onset before birth.

This occurrence in fœtal life is of great importance, for we are not accustomed to see at birth abnormalities such as in the older child are recognized to be of endocrine origin: indeed, it is stated that any perverted function of these glands cannot affect the fœtus, as such deficiencies are compensated for by the mother. It has been thought that perhaps arachnodactyly might be a fœtal gigantism of pituitary origin, the result of over-secretion of this gland. If we consider the three cases in which hereditary influences were marked we might argue that increased maternal secretion had been handed on to the child *in utero*, but in all these three instances other members of the family escaped: moreover, the mothers of these children did not show signs or symptoms known to be the result of such increase—they were not instances of acromegaly. Partial gigantism in the child persisting as in these cases into adult life without the development of true acromegaly would suggest that the activity of the morbid process ceased before, or at any rate shortly after, ossification was complete, and we should need to invoke such an explanation if we regard these cases of pituitary origin, for in the records of those examined in later life no signs or symptoms of acromegaly were found to be superimposed. We might suppose, perhaps, that during intra-uterine life the fœtus receives an abnormally increased amount of pituitary secretion, but that after separation from the mother it then depends upon the normal amount supplied by its own gland; and that thus the morbid process, removed at birth, cannot later produce acromegaly.

The enlargement of the lower jaw, the prominence of supraorbital ridges, the hypertrophied ears and many other signs, including even the muscular weakness, lend some support to the theory of pituitary hypersecretion; but it must be remembered that arachnodactyly is a partial gigantism only, for although the length of the complete skeleton is frequently increased, the elongation of the phalanges of hands and feet is relatively still greater. Moreover, it is most difficult to account for the thinning of these bones which has been found both by X-ray and post-mortem examination: this is directly opposed to the findings in gigantism or acromegaly in which the breadth is actually increased. Evidence afforded by autopsy is conflicting. Salle[21] found enlargement of the sella turcica, with the presence of a bony tumour growing out from the base of the skull in such a way as to press upon the hypophysis, which was, however, normal on microscopical examination. Borger[2], on the other hand, stated that in his case he found enlargement of the sella turcica posteriorly, thickening of the clinoid processes and flattening of the hypophysis: microscopically the posterior lobe was normal but the pars anterior and pars media were cystic, the epithelium was cubical in type, and large numbers of eosinophil cells were present.

My own clinical observations do not suggest that the pituitary is at fault. The gigantism is partial only, as in recorded cases, and though there is no marked thinning of the bones the breadth is certainly nowhere increased. Other features connected with pituitary disturbance are absent : none of the cases complained of headache, nor was optic atrophy present in any of them : no degree of temporal hemianopia was found, and the colour vision was normal in each case. Nor are there any signs or symptoms which might point to a hypo-secretion, the low systolic blood pressures and the decreased basal metabolic rate in one case are to be expected in such weakly children. On the other hand, by X-ray examination of the skull certain interesting features were noted. In each radiogram some change in the sella turcica was seen. In Case 3 it was not only small but appeared elongated, both anterior and posterior clinoid processes were thickened, but the opening was very little reduced in size, owing possibly to the general shape of the skull. In Case 4 the sella turcica was again smaller than normal and with a similar thickening of the clinoid processes, the opening was small but there was no elongation. In Case 1 a very marked reduction in size of the sella turcica and clinoid processes was seen. The radiograms did not appear to show any other abnormalities.

These appearances suggest that the pituitary body is smaller than normal, but in the light of clinical findings it does not seem that its function is in any way perverted. Lastly, the coexistence of so many varied congenital stigmata is unfavourable to the theory.

The same points apply with regard to other endocrine glands ; these cases do not suggest an abnormality of thyroid or other secretions.

(*b*) *A condition allied to mongolism.*

This suggestion seems to have a very doubtful foundation. Certainly abnormalities such as the highly arched palate, laxity of joints and ligaments, and especially deformities of the heart, are common to both, but arachnodactyly differs strongly from mongolism in other respects. The mentality is excellent. The head is commonly dolichocephalic whereas in mongolism it is brachycephalic and usually devoid of eminences. The mongolian hand differs markedly with its thick fingers rounded at the tips, short thumb and dwarfed little finger, and the characteristic large fissured tongue of later years is not seen in arachnodactyly. The oblique orbital fissures of the mongol have certainly been noticed in one instance by Rietschel, but the changes in the extremities of the bones found in arachnodactyly are unknown in mongolism. With regard to family history, the mongol is usually looked upon as an exhaustion product, a large proportion of the cases coming at the end of large families and being the offspring of mothers near the end of their child-bearing period ; this does not seem to be so in arachnodactyly, with one notable exception amongst my series, (Case 1), who was the last child of a family of fifteen and whose mother was forty-two years of age at the time of the patient's birth.

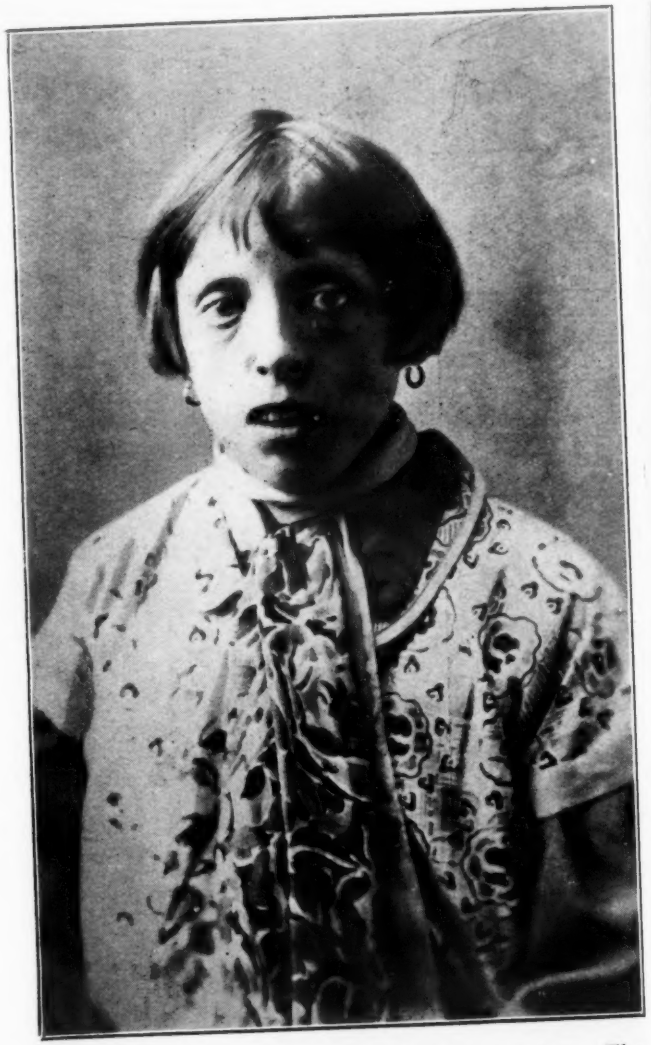


FIG. 1. Case 1. Showing the large lower jaw. The features here are very old for the age.

FIG. 2. Case 1. Showing the long slender and somewhat tapered fingers. The appearance of muscle wasting may be seen.

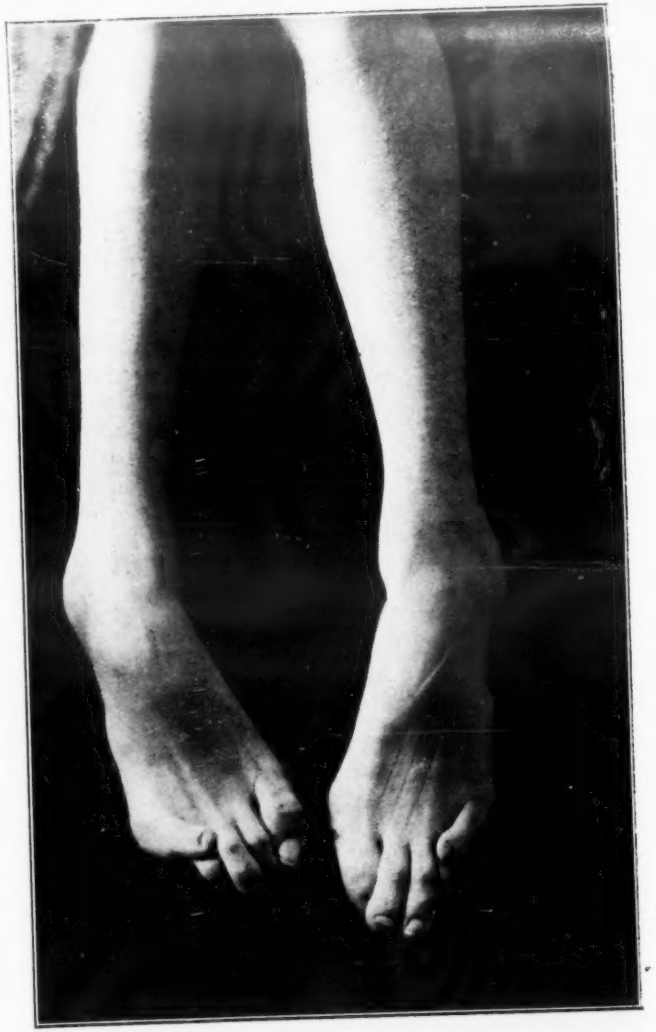


FIG. 3. Case 1. Showing the clubbed feet and deformed toes.

(*c*) *A form of hyper-chondroplasia.*

This term was originally suggested by Méry and Babonneix because skiagrams showed some activity of epiphyseal cartilages, but in later cases this has not been a feature, and in my series the epiphyses were normal. Nor can there be any connection with rickets though, as in the case quoted by Thomas[23], the two diseases may coexist: the early general indications of the latter are not seen in arachnodactyly, in which, moreover, dentition is normal.

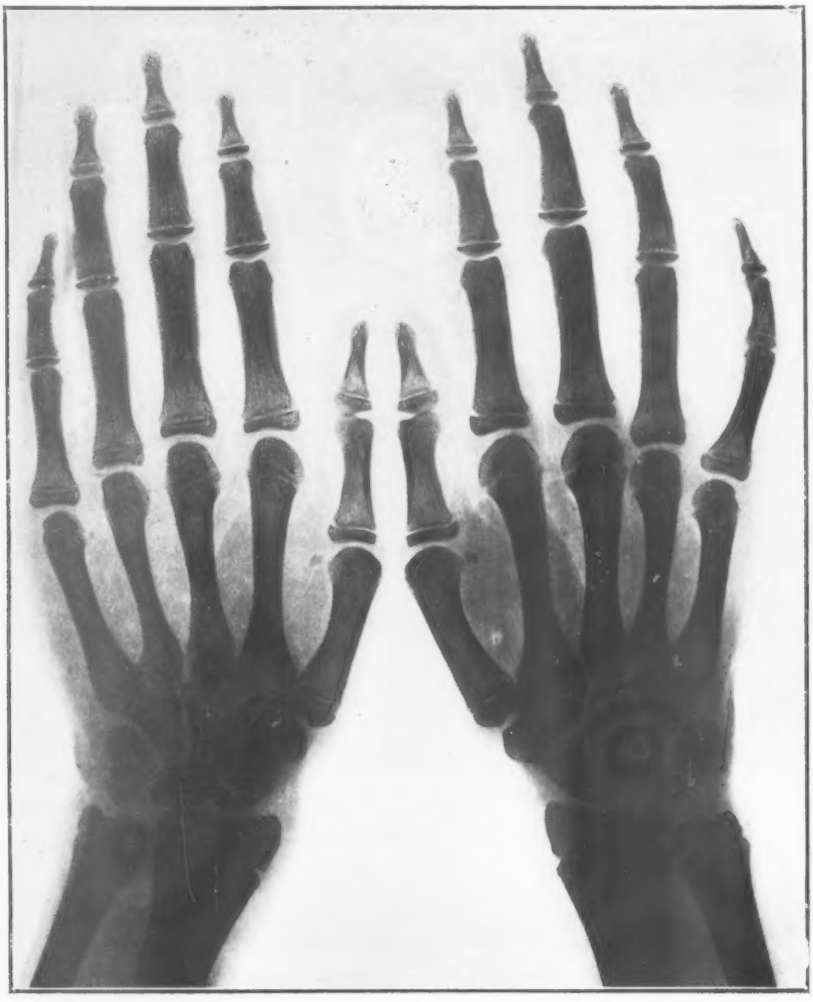


FIG. 4. Case 1. Showing the increased length of the phalanges; tapering is slight. No thinning nor rarefaction of bone is seen.

(*d*) *A form of primary muscular dystrophy.*

This suggestion was first advanced by a member present at the Medical Society of London in 1903 and again in 1917 by Thursfield who was the first to lay stress upon the atony and ill-development of the entire musculature.

That arachnodactyly is closely allied to amyotonia congenita is, I think, certain, though there appears to be no connection with other dystrophies. The comparison here made is chiefly based on Reuben's[17] account of 6 cases of amyotonia and a review of 136 others. Hereditary and familial influences are interesting. In 3 out of 26 cases of arachnodactyly both factors are

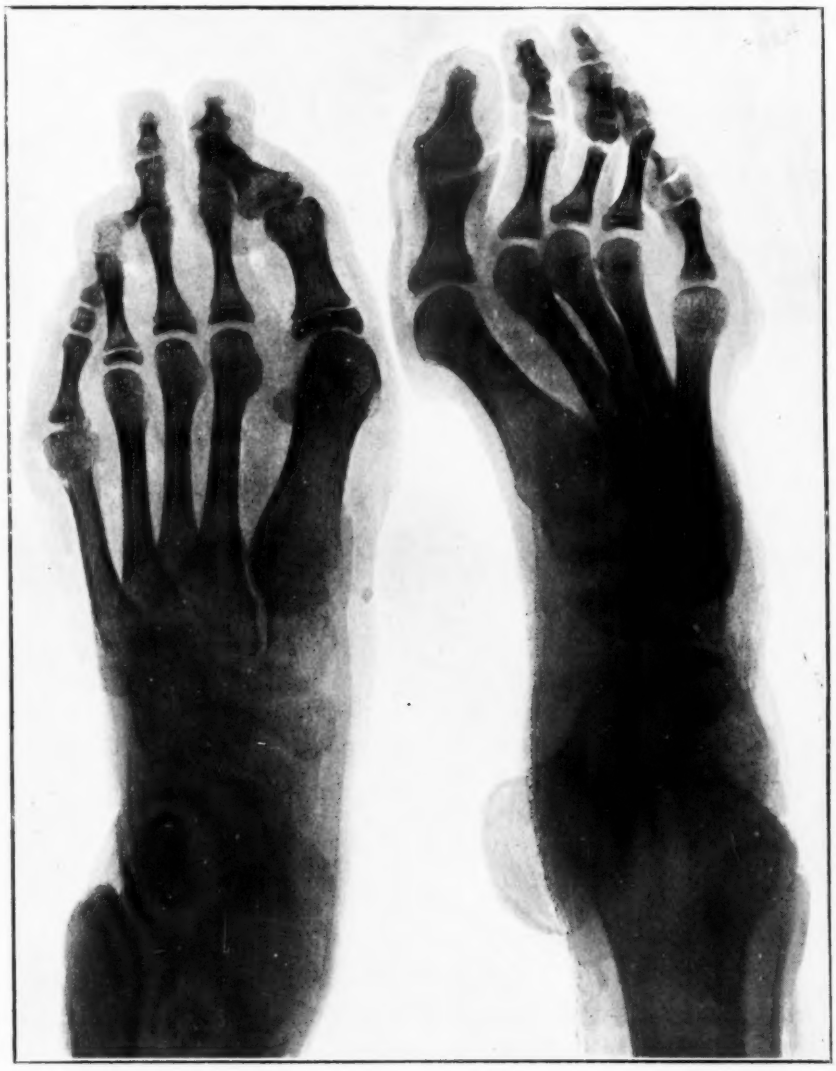


FIG. 5. Case 1. Showing the curious dwarfing of the middle phalanges of the little toes.

strongly marked, no mention is made in 6, and in the remaining 17 the histories are normal. Amyotonia congenita is also occasionally hereditary but more commonly familial, though Kerley and Blanchard[7] state that neither influence is usual. With regard to sex incidence, in arachnodactyly there were 10 males and 16 females, *i.e.*, a slight preponderance (61%) of the latter, whereas in amyotonia there is a corresponding increase in the male sex. The onset in

both is almost invariably intra-uterine, though amyotonia has been known to occur at a later period. The mentality found in the two conditions corresponds, being as a rule excellent. Congenital abnormalities and those resulting from muscular weakness occur in both, though in amyotonia they are comparatively rare: of these may be mentioned deformities and asymmetry of the skull, winging of the scapulæ, dislocations of the hip, club foot and various deformities of the thorax. Kyphosis and scoliosis are commonly found in both. One of

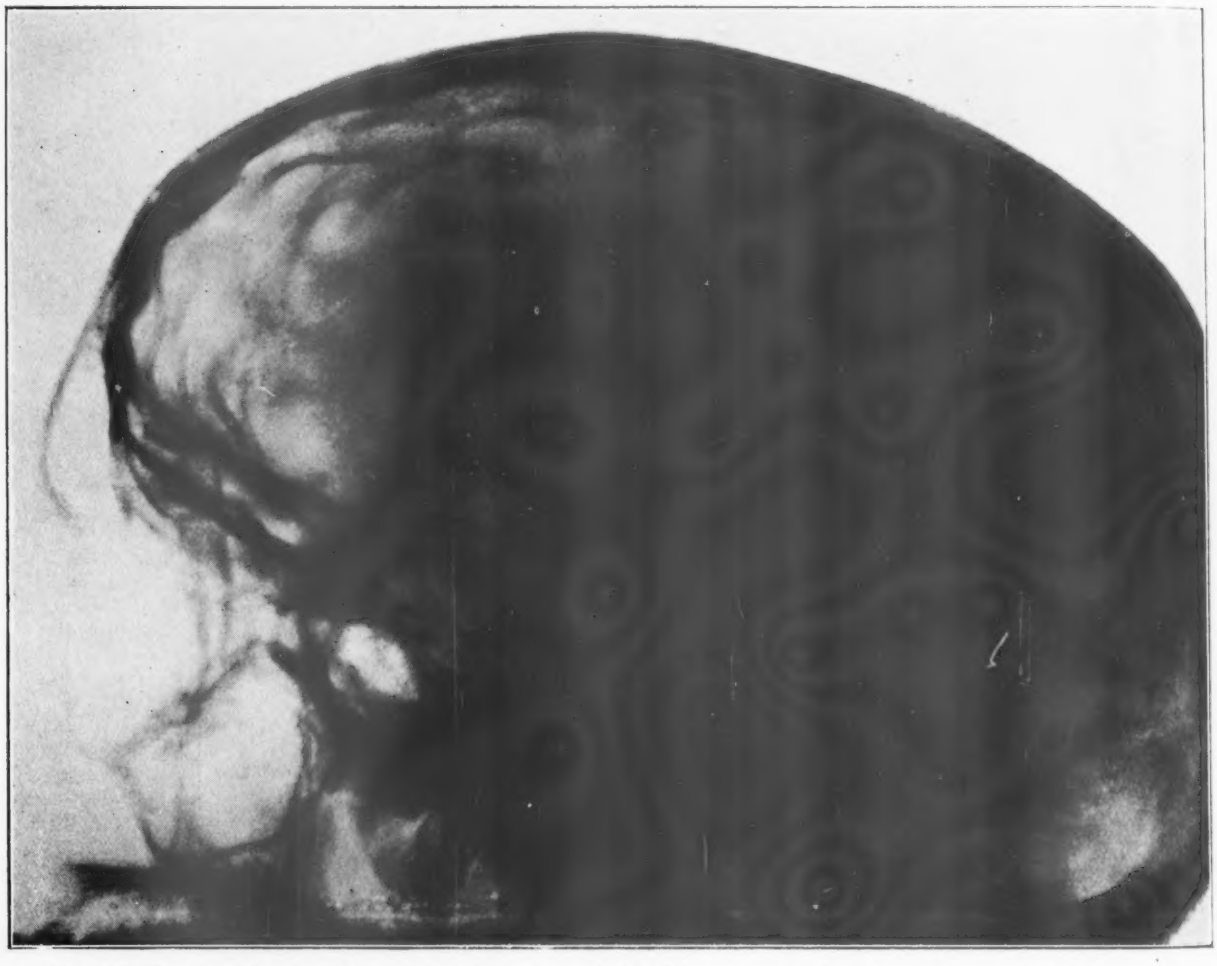


FIG. 6. Case 1. Showing the small sella turcica and clinoid processes; the latter are somewhat thickened.

the most interesting congenital abnormalities which occurs in a high percentage (27%) of cases of arachnodactyly, namely, congenital dislocation of the lens of the eye, is however not recorded in amyotonia by Reuben or other writers.

The great feature which these two conditions do undoubtedly share is the flaccidity of the musculature and to a slightly less extent relaxation of the ligaments. Of the 26 cases arachnodactyly there is mention of the muscles in no less than 19, which in 17 showed apparent atrophy. Laxity of the ligaments is a feature in 18 instances and not mentioned in 8. Resulting contractures

were present in 14. These figures may easily be too low, for in some of the recorded cases it is likely that no heed was given to the muscular system. It may also be noted that in the 9 cases in which some degree of muscular atrophy is not recorded, only 4 observers fail to mention the muscular system at all. Of the remaining 5, one (Fowler) had contractures of the forearm and marked hypotonicity, another (Rocher[19]) had contractures of the hamstrings and loose articulations. Achard[1] states that in his case the muscles were normal and contractures absent, but he does note an exaggerated mobility of joints, Pfaunder[14] speaks of a slenderness of soft parts and Lust's[8] case had flexor contractures of the fingers and toes. The muscles are therefore indirectly alluded to in a further 3 cases, and in yet another a 'slenderness of soft parts' seems suggestive. Thus the muscular system would appear to be affected in no less than 80% of total cases.

With regard to electrical reactions, Marfan[9] found a normal result but Dupérie, Dubourg and Guénard[5] noted a diminished response to faradism. Of my cases, Case 1, showed a slight but equal diminution of response to both faradic and galvanic currents, though a contraction was always obtained even from those muscles which appeared most wasted. In the other two cases the reactions were in every respect normal.

Organic disease of the nervous system is absent in both arachnodactyly and amyotonia, though Schlack in his account of a case of arachnodactyly described signs suggestive of affection of the posterior columns and pyramidal tracts, likening the case to Friedreich's disease. It is difficult to know in this sole instance whether such nervous phenomena are in any way related to the congenital abnormalities.

On the muscular findings alone arachnodactyly must surely be thought to possess one causal element in common with that of amyotonia, though the presence of some other factor or perhaps the selective action of this may be of importance. It is not suggested here that the two conditions are one and the same, but that there exists an exceedingly close relationship in the matter of ætiology; it is believed that an amyotonic state of the muscles is a constant accompaniment of arachnodactyly though the degree in which this feature is present varies. A combination of the two conditions each strongly represented in one patient has not been hitherto recorded, but two such instances are described later in this paper.

(*e*) *A fault in the embryo.*

Borger[2], in discussing the ætiology of arachnodactyly, has spoken of 'a partial gigantism caused by defective anlage or faulty predisposition of the entire organism, or perhaps an early nutritional defect of the embryo.' It has been shown that the condition starts during intra-uterine life, and it is interesting to note that dislocation of the lens is such a frequent feature of arachnodactyly, for this abnormality is believed to occur within the first three or four months of fœtal life. To form an opinion on this question is difficult. If a faulty predisposition is handed on to the embryo the condition becomes a matter of heredity and would probably be familial as well, but in

three cases in which these influences were present there were children in whom the condition did not appear: in each instance the heredity was entirely on the female side. Dupérie, Dubourg and Guénard[5] state that in their case the parents were very young, the father being only seventeen and the mother sixteen. In one instance (Marfan) a shock of an hallucinatory nature occurred early in the pregnancy. One case was four weeks premature and an only child. Miscarriages are noted by Marfan[9] and Salle[21], but for the most part confinements were normal. With the exception of one of my cases (Case 1) the pregnancies do not seem to have occurred either late in life or to have succeeded many others, which is opposed to the theory of a reproductive exhaustion put forward by Nobel[11]; this girl however, was the last child of a family of fifteen, her birth followed upon six consecutive still-births and the mother was forty-two years of age at the time. Tests made to determine any syphilitic infection were invariably negative.

Thus, beyond the hereditary factor and the occurrence of the condition in more than one but not all members of the families, there is little to note. Damage of an environmental kind must be supposed to be the result of some nutritional defect, physical or chemical in nature, such as could be brought to the embryonic tissue in the maternal blood, but in the large majority of cases the condition does not occur in more than one pregnancy and therefore the defect must be a temporary one. Recently much interest has been taken in the condition hypertelorism, first described by Greig, of which the main feature is an abnormal distance between the eyes. Though this peculiarity is not found in arachnodactyly there are several features common to the two conditions, such as the preponderance in the female sex, the congenital factor, arching of the palate, prognathous jaw, small mouth, large ears and other deformities. It is particularly interesting to note that in one case described by Braithwaite[3] the fingers and toes were thin and tapering and muscle tone was markedly deficient, recalling the contortions of amyotonia congenita. In hypertelorism also hereditary influence is occasionally though rarely evident. Although the two conditions differ in certain clinical manifestations, the fundamental factors in their ætiology must be closely allied.

Further observations upon ætiology.

Certain investigations were made in my series of cases but mostly yielded negative information. Renal function was found to be healthy; the urine by chemical, microscopical and bacteriological tests was normal, the blood urea was satisfactory and the concentration of this substance was excellent. The urinary diastase test gave normal results in two cases, but in the third (Case 1) the content was found to be 90 units. Although this figure proves that the ability of the kidney to excrete this ferment is good, it seems to suggest a hyper-secretion on the part of the pancreas, assuming that this organ is responsible for its secretion, a view which has been criticized. From a complete examination of the stools the pancreatic functions appeared to be normal and it is difficult to account for this high diastatic index. The liver also was healthy. Total and differential blood counts were normal. A Sachs-Georgi

reaction carried out in Case 1 showed no evidence of syphilis. The calcium content of the blood was normal. The decreased basal metabolic rate in this case has been mentioned. Blood pressures were found to be low; pulse pressures were high. The electrical reactions of the muscles have been described.

Of the various investigations made the only unusual findings obtained were those in connection with the sella turcica, and these have been discussed in that portion of the ætiology which deals with endocrine glands.

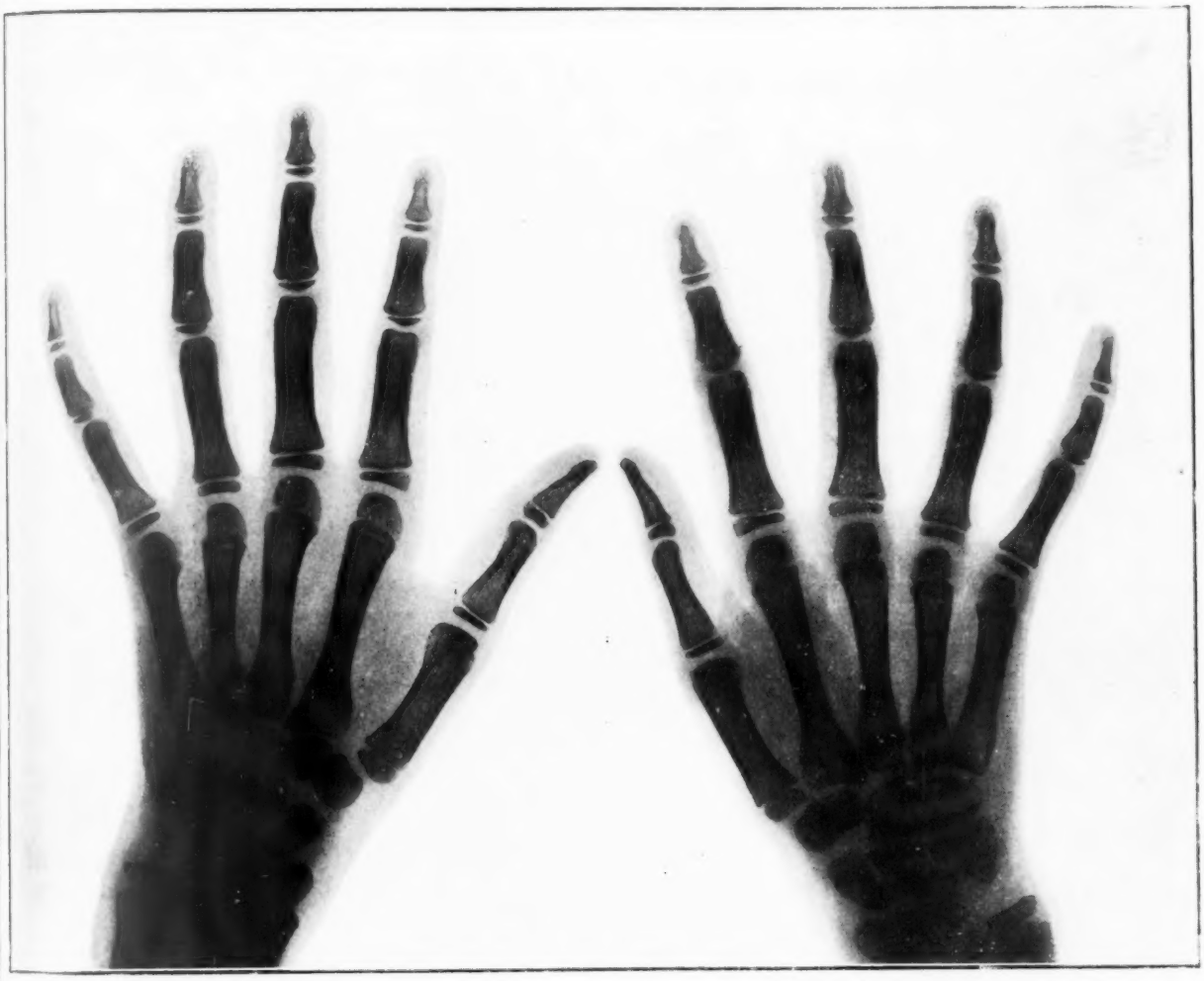


FIG. 7. Case 3. The length of the phalanges is increased. No further changes are apparent.

CLINICAL FEATURES.

The onset during intra-uterine life and the preponderance in the female sex have already been mentioned. It is convenient first to give from a survey of the literature the main clinical features to which the term arachnodactyly has been applied, then the observations on those points from my series of

cases, and lastly to discuss the many accompanying abnormalities under their respective headings.

A review of the literature shows that the striking characteristic consists of an abnormal lengthening of hands and feet especially noticeable in the fingers and toes. This is demonstrable not only as a real increase by comparison with children of the same age, but also as a relative increase by comparison with the total length of the child, although this is usually itself increased.

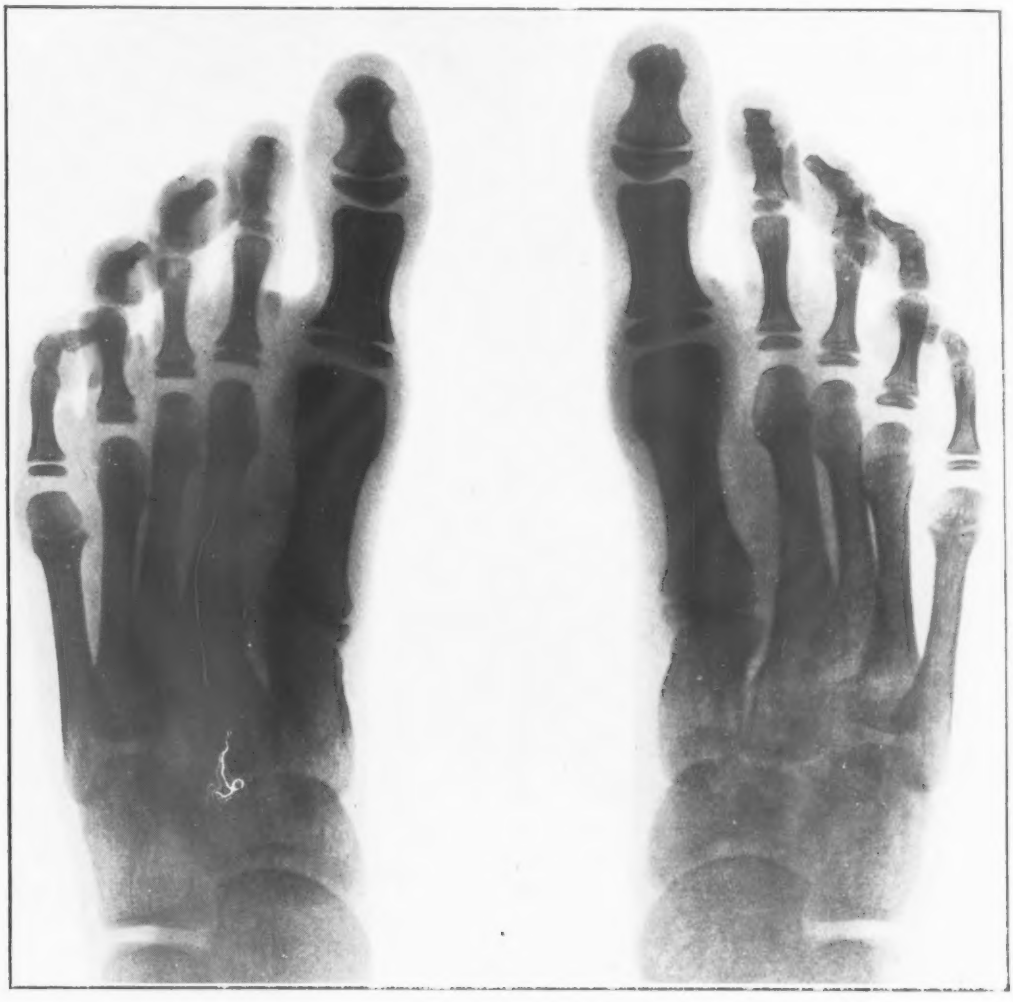


FIG. 8. Case 3. Bones are increased in length. No thinning nor rarefaction is seen.

Thus the child is abnormally tall for its age with hands and feet relatively long for its height. Equally striking is the thinning of the bones involved, and in the fingers especially there is frequently a tapering towards the distal extremities of the terminal phalanges resulting in a spidery appearance to which the term arachnodactyly is appropriate. The length and slenderness of the fingers are accentuated by a deficiency of the surrounding soft parts. The metacarpal and metatarsal bones share these peculiarities in many but not

all cases, and if so are usually affected to a lesser extent. The arms may escape, and any increase in length in them tends to be relatively greater in the forearms than upper arms, the elongation becoming more marked towards the distal end of the limb. The same is true of the legs.

Fingers and toes are not clubbed, though Thomas[23] notes this feature. Joints are very freely movable but structurally normal, the limbs are hyper-extensible without pain. Webbing of the fingers is not uncommon. Two cases of talipes calcaneus are described and one of hammer toes (Dubois[4]). Pes planus is common, pes cavus less so. Spurring of the os calcis is noted in 13 or 50 per cent. of total cases.

Whereas the height tends to be greater than the average for the age, the weight is considerably less. This is due to the deficient musculature and to the loss of subcutaneous fat. The consistency of the muscles is much altered and suggests that of adipose tissue.

My own observations differ in some respects from the foregoing description. In two of my cases there was a marked increase in height with a slight increase in weight also, and in two an equally marked decrease in both height and weight. Measurements were taken in each case of the lengths of the spine, upper arm, forearm, thigh and lower leg, and compared with those obtained from the average of a series of normal healthy children of the same age and sex (see Appendix, Table A). In the cases in which total body length was increased the figures obtained were in excess of the normal for the age, but where body length was decreased, they were smaller than the normal. The ratio of each measurement to the corresponding total height was therefore estimated. The results were very consistent and showed that the ratios were undisturbed, corresponding accurately with the normal (Table A). From this it is clear that in the long bones of the skeleton there is no progressive increase in length, for where elongation occurs in these bones it is shared equally amongst them and is in normal proportion to the corresponding increase in the height. There is therefore no partial gigantism.

In order to investigate the condition of the bones of the hands measurements were taken in millimetres from skiagrams of every phalanx and metacarpal in each of the cases ; these were then compared respectively with similar measurements obtained also from skiagrams of normal children of corresponding ages (see Appendix, Table B). It was found that there was a definite increase in length in every measurement taken with the exception of two distal phalanges and three metacarpals in the case of Case 1. It was also noticed that the figures obtained in Case 4 at the age of $7\frac{1}{2}$ years were mostly equal to, or greater than, those of the normal at the age of 14 years with which Case 1 is compared. This is so remarkable that these figures at 14 years are given in comparison with this case instead of those of a corresponding age. Individual discrepancies are obviously much greater in the two cases in which body length is increased, but even in those in which this is decreased there is a noticeable difference ; the figures shown in Table B are, I think, very striking, especially the comparison of the sum total of the phalanges and metacarpals with the normal. Since the figures in the cases in which height is decreased still show

an increase compared with the normal, it is obvious that the elongation in these bones is out of proportion to the body length. In each case ratios of the total sum of the phalanges and metacarpals of the second or longest digit to the respective body lengths were estimated and compared with the norma (Case 4 is again compared with the age of 14 years). The results prove that these bones exhibit a true partial gigantism (see Appendix, Table C).

In order to determine whether the elongation was confined to the phalanges or shared by the metacarpals, I estimated the ratios of the sum of the phalanges of each digit to the sum of the phalanges plus corresponding metacarpal bones in every case, and compared these with the normal (see Appendix, Table D). In Cases 3 and 4 (in which body lengths were increased) it was found that the phalanges of every digit were relatively longer to their corresponding metacarpal bone than in the normal child of the same age, the exact ratios being almost identical in these two children. In Case 1, however, the sum of the phalanges appeared to show a slightly smaller proportion of the whole, *i.e.*, the metacarpals were relatively longer. In the remaining case (Case 2), some variation was observed, but on the whole the increase seemed to be shared equally. Finally, taking the second digit only in each child, the ratios between individual phalanges and their corresponding metacarpals were estimated (see Appendix, Table E). The figures show that the greatest relative increase lies invariably in the terminal phalanx. In Case 1, both middle and proximal phalanges were also increased relatively, but in the other cases there was some variation.

With regard to the feet, to obtain measurements accurate enough to draw conclusions is practically impossible. Owing to accompanying deformities, such as talipes, foreshortening appears in the photographs and the proximal ends of metatarsals especially are frequently blurred. Appearances suggest that a similar state of things obtains as in the hands.

By X-ray examination it was also observed that the thinning of the bones was more apparent than real, nor is tapering very evident, the deficiency of soft parts is probably largely responsible for the spidery appearance. No rarefaction was observed nor was there any evidence of advancement of ossification.

As in recorded cases there was a marked freedom of movement at the joints with a laxity of ligaments. The muscular condition was striking. In two cases the apparent wasting was general in distribution with the exception of the face which entirely escaped, but the loss of power was not in proportion though Case 2 was a very weakly specimen.

In addition to the peculiarities of hands and feet, a host of abnormalities in other parts of the body has been described, many of which I have observed in my series of cases.

Mentality. This is mentioned in 19 cases, of which 17 (90%) are normal. In two of my cases it was impaired during the first few years only.

Teeth. In two cases dentition was delayed, early caries was noted in three and in one (Rominger)[20] there was a double row of teeth in the lower jaw. The teeth are mostly normal.

Speech. Occurred late in 4 cases, some impairment in 4 others.

Skin. Mentioned in 11 cases, in 3 described as pale, in 3 as dry and fine, in 5 there was no peculiarity.

Hair. Described variously as being thick and dry, coarse, straight, and abundant. No type is peculiar to the condition.

Head and Face. Abnormalities of the skull are extremely common, being present in 17 or 65% of all cases. In 6 the shape was found to be of the dolichocephalic variety, in 1 only it was brachycephalic. Other deformities found

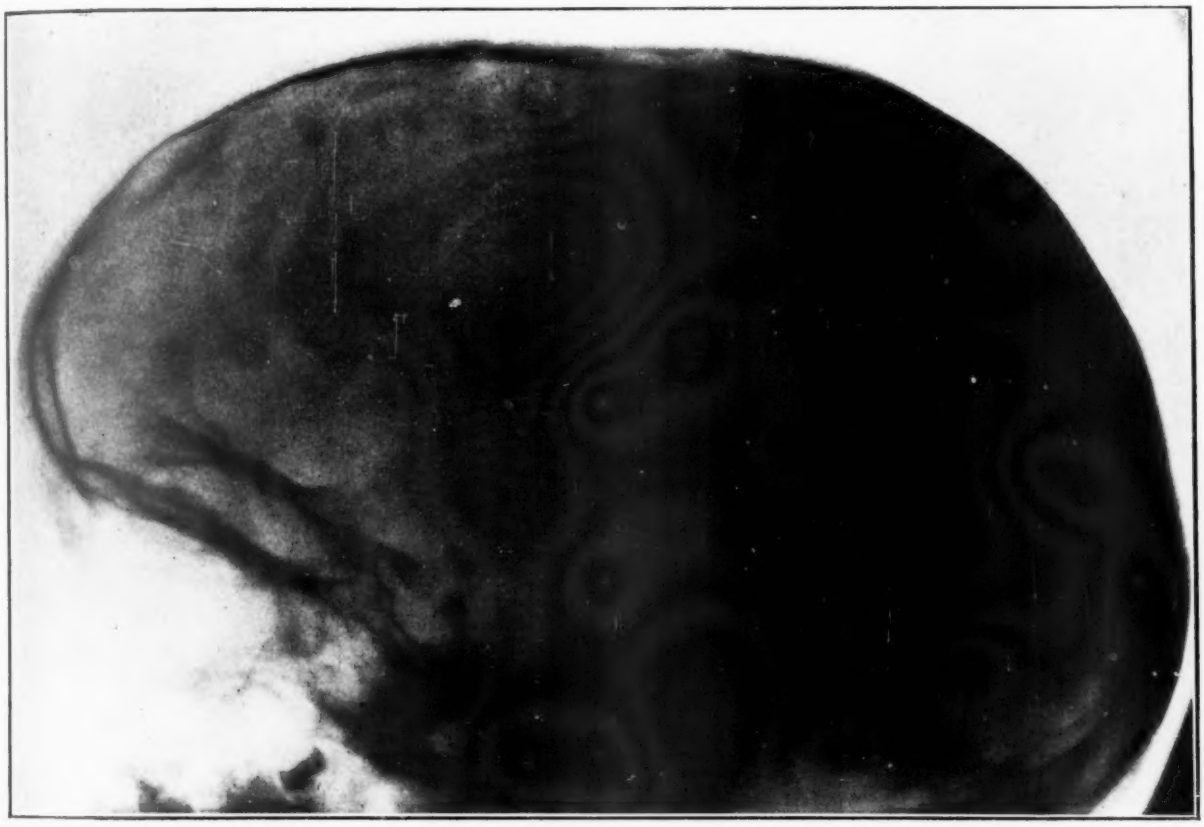
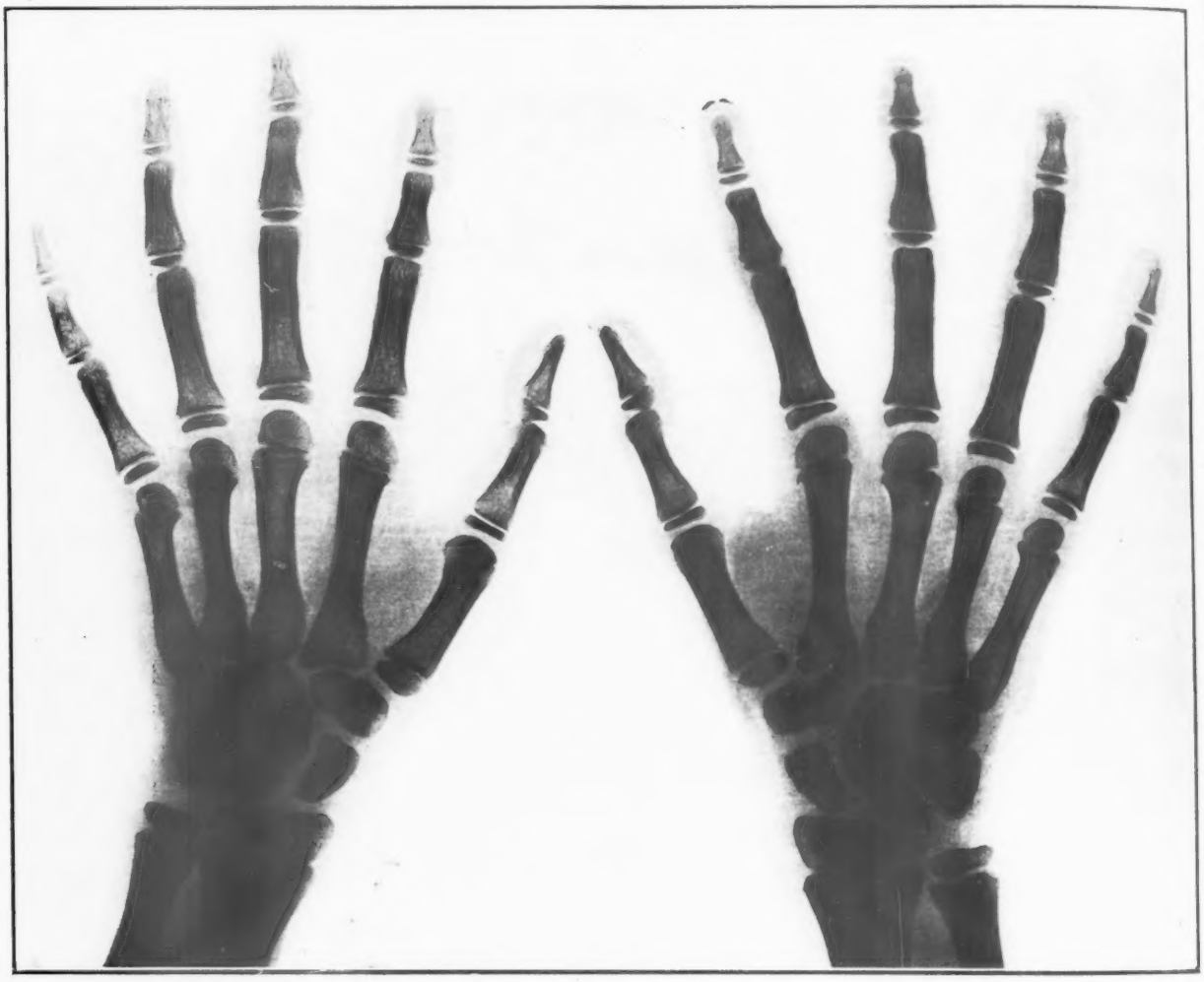


Fig. 9. Case 3. Showing a curious elongation of the sella turcica; the clinoid processes are thickened; the opening is very little reduced in size.

are :—Asymmetry in some form in 3, relative smallness of the skull in 2, prominence of the chin in 5, prominent supra-orbital ridges in 4, bossing of the frontal eminences in 5, patency of the anterior fontanelle in 2, depression of the base of the skull in 1, prominence of the nose in 1, poor development of the base of the nose in 1, and of the inferior maxilla in 1. There was no mention of the skull or head in 5 cases, in 4 it was described as normal. The face was mentioned in 8 cases as being old for the age, the lips small in 4, the whole face small in 1, in 1 the nose was large and in 1 the neck was short. Marked naso-labial folds were also noted, the oblique axes of the orbital fissures of mongolian type were present in 1 case. Salle mentioned a large tongue. The

vault has been found to be thin at autopsy, and in 2 cases the roofs of the orbits projected backwards unduly into the interior of the skull.

Thorax. Abnormalities are present in 13 or 50% of cases: the funnel shaped chest was found most common by occurring in 6 (23%), projection of the lower sternum with flattening of the whole or part of the chest wall in 3. Pigeon breast was also seen. Rarefaction of the ribs was described in 1 case.



IG. 10. Case 4. The increase in length of the phalanges is very marked and actually bears comparison with Case 1 who is 6½ years older.

Scapula. Described as winged in 4 cases, long in 2, rarified in 1, normal in 4. Not mentioned in 16.

Spine. A kyphosis alone is common (45%), but there may be a scoliosis or a combination of the two. These are probably always the result of muscular weakness. In 1 case the pelvis was asymmetrical.

Palate. This was noted as highly arched in 10 cases. In 1 there was a median cleft in the hard portion. It is possible that the highly vaulted palate

occurs more often than the figures suggest since it is an abnormality which has specially to be looked for.

Ears. Deformities were mentioned in 17 cases all of which affect the external ear only. Most common were a general enlargement of lobes especially. deficiency of cartilage, and over-development of the crus helicis. Less common are over-development of the anti-helix, tragus, and cartilage, depressions in the concha and bad definition of the crus helicis, anti-helix and lobules. A

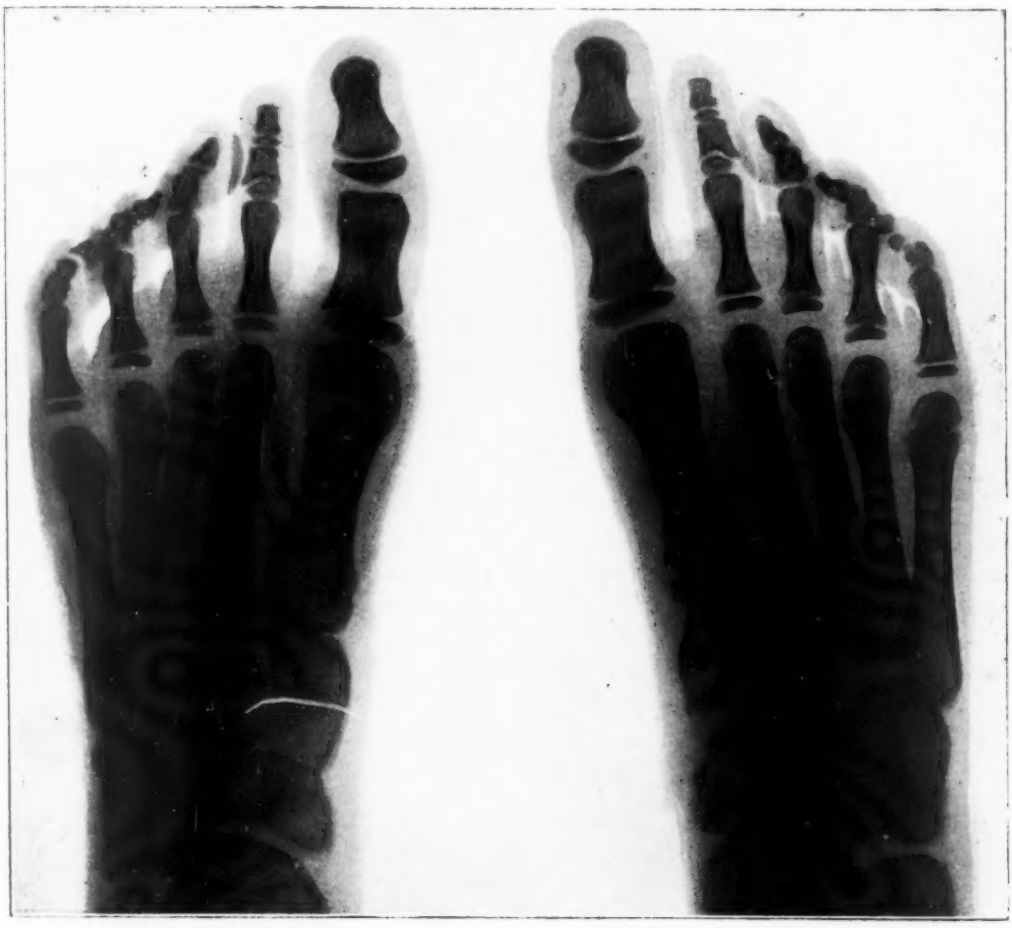


Fig. 11. Case 4. The bones show some increase in length. No other abnormality is present.

division of the lobules into separate portions has also been described. A combination of abnormalities is usual.

Eyes. These are amongst the most interesting of all accompanying congenital deformities. Not only is their occurrence in some form or other very frequent, being noted in 50% of all cases, but in addition one particular abnormality, that of dislocation of the lens, occurs most often. In conjunction with other congenital maladies of the eye this condition is extremely rare, yet it is in arachnodactyly a feature in fully half of those cases which show ocular abnormalities. Of 26 cases the eyes showed some peculiarity in 13, and of

these 7 had luxation of the lens. In many the eyes have probably escaped examination, in 9 they are not mentioned, and once again it is possible that the incidence of this particular feature is higher than the figures suggest. It is also interesting to note that dislocation of the lens never occurred as a single abnormality. It was accompanied by iridodonesis in 4 cases, in 2 of which congenital hydrophthalmos was also present. The pupils were frequently very small and the globes deeply set. Squint occurred often, nystagmus

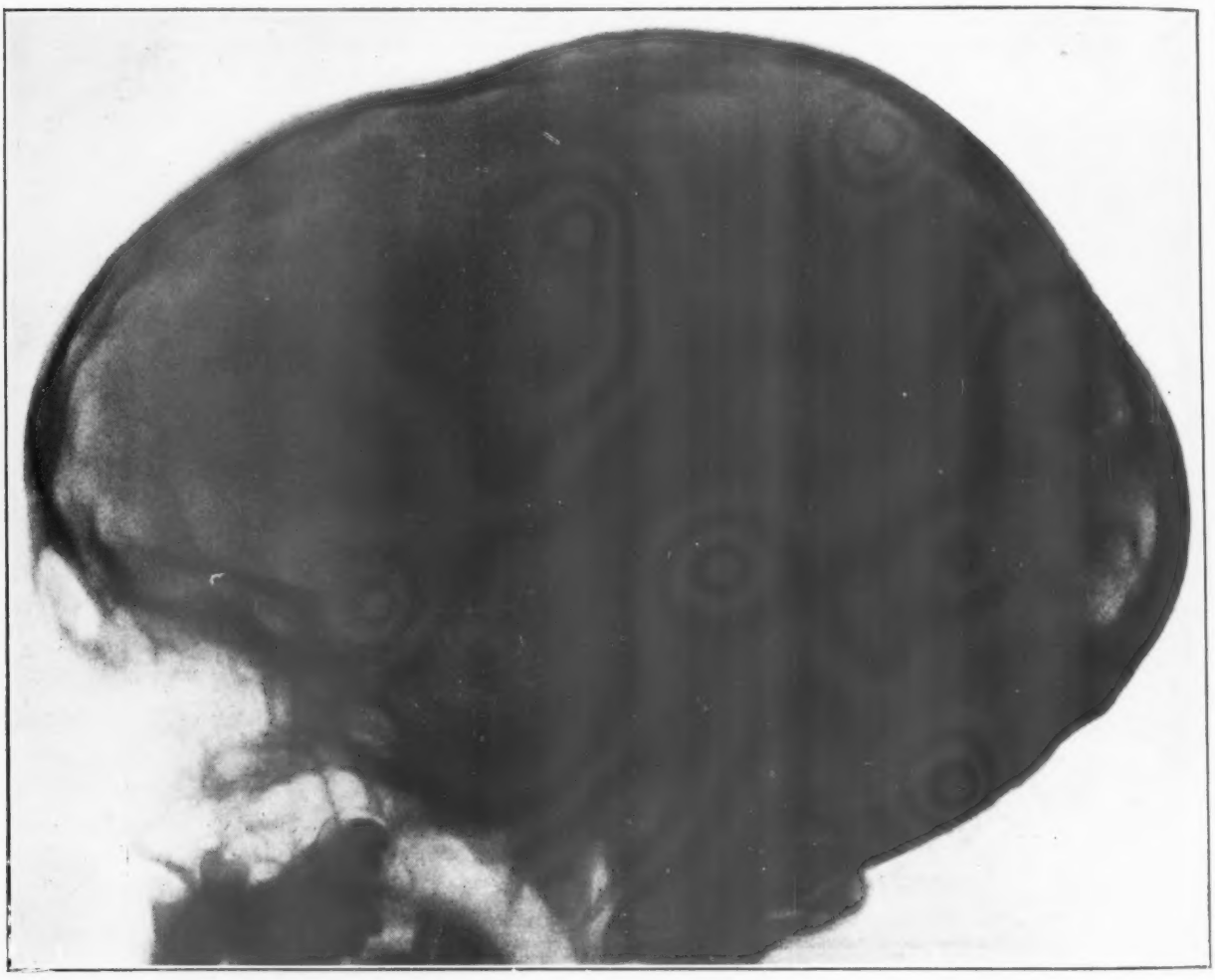


FIG. 12. Case 4. The sella turcica is reduced in size; clinoid processes are thickened.

occasionally. A persistent pupillary membrane was mentioned in 1 instance. High degrees of myopia occurred, and amblyopia, enlargement of the cornea, and shallowness of the anterior chamber were recorded. Optic discs apart from myopic appearances were normal; no instance of congenital cataract was found. Accompanying peculiarities such as œdema of the eyelids, deficiency of eyelashes, marked epicanthic folds, and variations in the size of the two orbital fissures were also mentioned. Rietschel in his description of the

slanting axes of mongolian type made no further reference to the eyes. A list of the various ocular abnormalities, showing their total and relative incidence, is shown in Table I.

TABLE I.

OCULAR ABNORMALITIES IN ARACHNODACTYLY (26 CASES).

Abnormality	No. of cases	Total incidence	Relative incidence
Dislocation of the lens	7	27%	54%
Iridodonesis	5	19%	38%
Small pupils	5	19%	38%
Deeply set globes	4	15%	30%
High myopia	3	11%	23%
Squint	3	11%	23%
Nystagmus	2	8%	15%
Congenital hydrophthalmos	2	8%	15%
Enlargement of the cornea	1	4%	8%
Shallow anterior chamber	1	4%	8%
Persistent pupillary membrane	1	4%	8%
Amblyopia	1	4%	8%
Fundus oculi	Normal except for myopic appearances.		

Total number of cases, 26. Numbers showing abnormalities of the eyes, 13 or 50%. Number in which there is no mention, 9.

Lungs. At autopsy Borger found a deficiency of the middle lobe of the right lung, and in the left a large lingula was present. Piper and Irvin-Jones found a very small middle lobe in the right lung and the left consisted of one lobe only. Salle's case showed no defect. Death was due to pneumonia in each instance. The liability to this disease is great since the bony thorax is so frequently deformed.

Heart. Affections of the heart were mentioned in 9 cases, of which 5 are considered to be congenital in type. In 2 a patent foramen ovale was seen at autopsy and in a third the interauricular septum was deficient. Valves were normal in each case. Amongst my series no abnormalities were found.

Viscera. Salle found a splanchnomegaly or increased length of the gut. With this exception the viscera are normal. No defect of the abdominal wall was recorded.

Ductless glands. Apart from Borger's account of the pituitary body and the X-ray findings of the sella turcica in my cases, both of which have been mentioned, there is no evidence of abnormality of any ductless gland. Borger also described the external genital organs as small in one instance, but in another the mons veneris and labia were very large, a feature noticed by Pfaunder.

Nervous system. With the exception of Schlack's account which is described above (see Ætiology, section *d*) no abnormalities of this system are on record.

Differential Diagnosis.

This presents no difficulty if the hands and feet are examined, the symmetrical involvement and the absence of bony disease will exclude other conditions. It may be distinguished from infantile paralysis, obstetrical and diphtheritic palsies by the absence of organic changes in the nervous system. In cases of amyotonia congenita, in which the muscular condition may completely dominate the picture, an accompanying arachnodactyly might remain undiagnosed unless the possibility of its existence be remembered. Wasting may suggest tuberculosis which may, of course, be present at the same time. The points which should distinguish mongolism and acromegaly have been mentioned. Syphilis is excluded by the Wassermann or other test.

Conclusions.

1. Arachnodactyly is a clinical entity of rare occurrence. It is congenital in origin, and its onset probably takes place during the early months of intrauterine life. It is more common in females than in males in the ratio of 3 to 2.

2. Heredity is an important factor in causation though apparently absent in the majority of cases. The condition is not usually familial though it may occur in more than one member of a family.

3. It is not a result of parental reproductive exhaustion though one case suggests this possibility; neither is there in this respect nor from clinical findings a connection with mongolism. Pathological evidence shows that it is not a form of hyperchondroplasia.

4. Radiograms showing abnormal appearances of the sella turcica are described in three cases, but since no clinical evidence suggests a perversion of pituitary secretion the view is held in this paper that the functions of the pituitary are normal, nor are there grounds for supposing an abnormality of any other endocrine glands.

5. The functions of those organs especially connected with metabolism such as the liver and pancreas, and with excretion such as the kidney, have been investigated. No defects of any sort were found.

6. Clinically the condition exhibits a true partial gigantism, as is proved by a comparison of measurements obtained by X-ray photographs with the normal. The increase in length is present especially in the bones of the hands, of which the terminal phalanges are the most affected.

7. The characteristic deformities of the hands and feet never occur alone, other congenital stigmata are always to be found. The frequent occurrence of abnormalities of the eyes is emphasized, particularly that of congenital dislocation of the lens.

8. An atonic state of the muscles is constant and may be regarded as a part of the condition. This conforms in all essentials to that found in amyotonia congenita though it varies greatly in degree in different patients. It is suggested here that though the two diseases are not one and the same, the fundamental factors in the causation of both are very closely allied.

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(*For Appendix, see p.* 210).

APPENDIX.

AUTHOR'S CASES: CLINICAL RECORDS AND TABLES A—E.

Case 1. D.W., female, aged 14 years.

Family History. Father died of cerebral abscess, mother healthy; no history of nervous or muscular disease in any relation. Mother had 15 children, 9 of whom died, 6 being consecutive still-births; remainder are alive and well.

Past History. Last child of family, following 6 consecutive still-births; born at full time and healthy at birth. Sat up, talked, walked and cut her teeth at the usual times; no illnesses during infancy. Mother was 42 years of age at time of patient's birth.

On examination. Extremely thin in all parts except the face; intelligence and speech normal; can sit up and remain erect with ease, but walking is limited by deformities of the feet. The skin is pale, hair abundant but not coarse. There is a degree of wasting and atony of the musculature in general excepting the face; this is most marked in the limbs especially the hands. Loss of power is present but does not correspond in degree; ligaments are lax though hypotonicity is not extreme, no grotesque positions are possible. The fingers are very long, thin, and somewhat tapered, the ring and little digits are slightly contracted; no webbing, no clubbing nor acrocyanosis; nails are normal. Apart from the fingers the hands are narrow but do not appear unduly long; muscular wasting is marked both upon dorsal and palmar surfaces. Forearms and upper arms also appear long but as measurements show this is apparent rather than real, moreover their ratios are unaltered. Muscular wasting is marked and is also seen in the shoulder girdle.

Both feet clubbed and their relative length difficult to estimate; toes very thin and deformed, but no contractures present; no clubbing nor webbing, os calcis not spurred. Both lower legs and thighs are very thin, but not unduly long; all muscles wasted, especially glutei; there are no contractures; the external malleoli are prominent, patellæ of normal size but highly placed. The spine shows a slight dorsal kyphosis; both scapulæ are winged but of normal size and shape.

Radiograms of the hands suggest an increased length of phalanges and metacarpal bones which is confirmed by measurements, tapering is very slight and thinning not marked; no rarefaction and ossification normal. Feet show the curious dwarfing of the middle phalanges of the little toes peculiar to this case, the talipes causes foreshortening of metatarsal bones especially, their proximal extremities being very faintly outlined, in the right foot they are superimposed; thus accurate measurements are impossible.

The skull is dolichocephalic in shape, occipito-mental diameter is 9½ in., greatest circumference 21½ in. No asymmetry but jaw large and of the nutcracker type; fontanelles closed; supraorbital ridges normal; eyes not deeply set nor far apart; the palate narrow and somewhat arched; teeth normal; tongue not enlarged. Face not small but features are those of an adult; mouth and lips large; ears larger than normal, cartilage soft and deficient, lobules poorly differentiated, drums normal, hearing unimpaired. Radiogram of skull shows a marked reduction in size of the sella turcica and clinoid processes, with some thickening of the latter; no other abnormality. Chest somewhat flattened but otherwise normal, the rib epiphyses not enlarged. Lungs normal, no evidence of deformity of heart, viscera apparently unaffected, no defect in abdominal wall. Nervous system intact, all deep reflexes abolished but no true paralysis exists. Eyes normal, vision emmetropic, no dislocation of the lens, colour vision normal. No apparent affection of thyroid, thymus or other gland; external genital organs normal, early features of puberty present.

Urine normal; renal efficiency tests satisfactory; an estimation of the diastatic content of the urine showed that 1 c.cm. of urine contained 90 diastase units (discussed above). Fæces on a mixed diet showed complete digestion of all elements, especially no evidence of pancreatic deficiency; no abnormal pathogenic organisms found in cultures. Blood calcium content normal, amount of bilirubin present in the serum also normal; complete blood count satisfactory; a Sachs-Georgi reaction negative. Estimation of the basal metabolism showed a decrease in the rate of 30·6% compared with normal. Systolic and diastolic blood pressures low, but the latter was relatively high giving a small pulse pressure of 32 mm. Hg. Electrical reactions of

muscles showed a slight but equal diminution of response to both faradic and galvanic currents; the most atrophic muscles showed no reaction of degeneration, a moderately strong faradic stimulation caused much pain.

Case 2. K.S., female, aged 3 years.

Family History. Nothing of any interest to record.

Past History. Eighth child of a family of ten. Born at full time and healthy, though the long fingers were noticed; progress normal up to nine months when the amyotonic symptoms seem to have come on suddenly.

On examination. Thin generally; listless and utters no intelligent sounds but seems pleased with objects shown to her; quite unable to raise head from pillow; both arms are in full pronation, slightly abducted and flexed at the elbows; knees are flexed with some spasm; no contractures are present. no tremors, fibrillary twitchings nor choreiform movements. Symmetrical wasting of all muscles of both upper and lower limbs is marked, those of neck and shoulder girdle are slightly affected; in the face, trunk, and chest muscles normal. Loss of power is in proportion, in the limbs it is almost but not quite complete; in affected areas the recognition of muscle apart from adipose tissue is exceedingly difficult. Electrical reactions not tested. Hypotonicity marked but not extreme, limbs may be hyperextended without pain. The hands, especially the fingers, appear absurdly long, very thin and somewhat tapered towards the extremities; no webbing nor clubbing, nails are normal; muscles of the thenar and hypothenar eminences very wasted. The feet and toes are also of abnormal length, the calcaneus is markedly spurred; there is no tapering; muscles less affected than those of hands. Remaining parts of body do not appear unduly long and as measurements prove, their normal ratios are unaltered. Radiograms of hands show increased length, and measurements compared with the normal prove that this is present in every phalanx and metacarpal; moreover, as in other cases, this increase is out of proportion to the height; the terminal phalanx is the most effected; no rarefaction, ossification normal. Those of the feet do not suggest so marked an increase in length of the bones, accurate measurements are not possible; no tapering, no thinning, no rarefaction; ossification normal.

Skull normal in shape and size, fontanelles closed; the palate narrow and very highly arched; radiogram shows no abnormality. The face very small, features have an old appearance; ears have large lobules but otherwise normal; teeth are decayed but not malformed; skin and hair show no peculiarity. The chest is pigeon-breasted, there is a fibrotic condition at the base of the left lung; epiphyses not enlarged. Scapulæ not winged, patellæ normal, spine shows lumbar kyphosis only. Heart unaffected; abdomen prominent but no viscera felt. Nervous system intact, all deep reflexes abolished, but no paralysis present. Eyes normal in every respect. No apparent affection of thyroid, thymus or other gland; external genital organs normal.

This child developed an acute pneumonia and died before further investigations could be carried out. An autopsy was not performed.

Case 3. K.A., female, aged 5 years, 8 months.

Family History. Mother (now deceased) had very long and thin fingers from birth, and used to wear an unusually large size of boot; she was able to put her limbs into grotesque positions easily and without pain and she had a bilateral dislocation of the lens; she was 5 feet 8 inches in height and exceedingly thin; her weight is not known. She was the thirteenth child of the family and the only one affected, her father and mother were normal; she herself had four children of whom the two youngest were affected.

Past History. Youngest child of the family. Born at full time, healthy though the peculiarities of hands and feet were noticed at the time; except that speech was unintelligible until three years progress was normal.

On examination. Very thin and tall, speaks in a slow deliberate way but mentality is normal. Muscular wasting seen in palms of hands and to a less extent in soles of feet; in forearms and lower legs it is very slight and in upper arms and thighs it is absent. Scapulæ not winged but seem long; slight lumbar kyphosis; remainder of the musculature is unaffected. Loss of power only in the hands very slight; marked hypotonicity present, ligaments are lax and extreme movements are possible without pain; both Achilles tendons slightly contracted

Hands appear very long, especially fingers which are thin and moderately tapered, slight but definite syndactyly present; no clubbing; nails are normal. No contractures or further deformities. Forearms and upper arms appear long and measurements show a marked increase above the normal, but ratios to the total body length are not disturbed, the increase is therefore in proportion to the height. Feet long and thin and toes slightly tapered; no clubbing; nails are normal. Os calcis spurred. Both feet plantar-flexed but full extension possible; no webbing; slight pes planus. Child takes size 13 in boots. Lower legs and thighs show the same proportionate increase in length as upper limbs; the external malleoli are prominent, patellæ are of normal size but highly placed.

Radiograms of hands show increased length, proved by measurements to be very marked and out of all proportion to the height, terminal phalanx is again most affected. There is some degree of tapering but no thinning, rarefaction absent and ossification normal. In feet this tapering is not evident, the bones appear to be increased in length.

Skull markedly dolichocephalic but symmetrical in shape; frontal bones, supraorbital ridges and lower jaw prominent, the palate narrow and highly arched, teeth normal, the tongue not enlarged. Face is old for age, lips very small, both ears very large with deficiency of cartilage and depressions in concha, crus of the helix badly defined, drums normal. Radiogram of skull shows a curious elongation of the sella turcica which is somewhat small in size, clinoid processes thickened but opening very little reduced in size. No other abnormality is seen. Chest normal, epiphyses not enlarged. Lungs normal, heart shows no deformity. Viscera unaffected. Nervous system intact; eyes show a bilateral dislocation of the lens with high degree of myopia, slight internal strabismus on the right side, colour vision is normal. No affection of thyroid, thymus or other gland; external genital organs normal.

Urine normal, also renal efficiency tests; diastatic content urine not raised in this case. Complete examination of stools satisfactory; blood counts normal, blood pressures low, Wassermann test not carried out; electrical reactions of muscles show no abnormality.

Case 4. O.A., male, aged 7½ years.

Family History. Brother of Case 3.

Past History. Third child of the family, born at full time and was healthy though the long hands and feet were noticed; speech was unintelligible until three years; otherwise progress normal.

On examination. Tall and thin, speaks in the same slow manner as sister but mentality normal. Apparent wasting of all muscles of forearms, hands, lower legs and feet, especially noticeable is atrophy of glutei; remainder of musculature unaffected, though there is slight lumbar kyphosis, and scapulæ which appear long have a tendency towards winging; both Achilles tendons slightly contracted. Loss of power in the hands, and slightly in forearms and lower legs; ligaments lax and hypotonicity marked, extreme movements can be carried out without discomfort. Hands, especially fingers, appear very long and thin; a slight degree of webbing, no tapering nor clubbing; nails normal, no contractures present. Forearms and upper arms longer than normal but in direct proportion to height. Feet long and thin but toes do not taper; no clubbing; nails are normal. Os calcis spurred, slight pes planus; takes size 1 in boots. Thighs and lower legs long but in proportion to height, external and internal malleoli prominent, patellæ of normal size but extremely highly placed. Radiograms of hands show same features as sister (Case 3) and measurements are actually comparable with those of a normal child of 14, *i.e.*, 6½ years older. Radiograms of feet also similar to those of Case 3.

Skull also corresponds in every detail, the face old, the upper lip small and sunken and the abnormalities of ears are exactly similar. Radiogram shows sella turcica reduced in size with small opening, but no elongation as in the previous case; clinoid processes thickened. Chest somewhat funnel-shaped, with prominent lower sternum; epiphyses not enlarged; lungs normal, heart shows no deformity. Viscera unaffected. Nervous system intact. Eyes show bilateral dislocation of lens with high degree of myopia; slight internal strabismus on left side; colour vision normal. No affection of thyroid, thymus or other gland; external genital organs normal.

Urine normal; renal efficiency tests satisfactory; diastatic content of the urine not raised; examination of stools shows no defect; blood counts normal; blood pressures low but higher than in the previous case; Wassermann test not performed. Electrical reactions of muscles show no abnormality.

TABLE A.

SHOWING MEASUREMENTS OF LONG BONES IN INCHES WITH RATIOS TO HEIGHTS.

	Case 1				Case 2				Case 3				Case 4			
	Measurement		Ratio to height		Measurement		Ratio to height		Measurement		Ratio to height		Measurement		Ratio to height	
	Patient	Normal	Patient	Normal	Patient	Normal	Patient	Normal	Patient	Normal	Patient	Normal	Patient	Normal	Patient	Normal
	in.	in.	1 to :-	1 to :-	in.	in.	1 to :-	1 to :-	in.	in.	1 to :-	1 to :-	in.	in.	1 to :-	1 to :-
Total body length	53	57·5	—	—	32	36	—	—	47	39½	—	—	51	47½	—	—
Spine	24	25	2·2	2·3	15	17	2·1	2·1	19	16½	2·47	2·4	21	20	2·4	2·38
Upper arm ...	10½	12	5·0	4·8	5	5½	6·4	6·54	7¾	6½	6·0	6·0	9	8¼	5·7	5·75
Forearm ...	8½	9	6·2	6·4	4¼	4¾	7·5	7·36	7¼	6	6·4	6·6	7½	7	6·7	6·8
Total arm ...	19	21	2·8	2·74	9¼	10¼	3·45	3·51	15	12½	3·1	3·1	16½	15¼	3·1	3·1
Thigh ...	16	18	3·3	3·2	8½	9½	3·7	3·62	13½	11	3·5	3·6	14½	13½	3·5	3·5
Lower leg ...	12	15	4·41	3·83	7	8	4·6	4·5	12¼	10	3·9	3·95	13½	12½	3·8	3·8
Total leg ...	28	33	1·9	1·7	15½	17½	2·06	2·05	25¾	21	1·8	1·88	28	26	1·8	1·8
Foot	7½	9	7·0	6·4	5¾	5¼	5·56	6·85	8	6½	5·8	6·0	8½	7¼	6·0	6·5
Weight ...	50 lb.	100 lb			16 lb.	20 lb.			42½ lb	42 lb.			51½ lb.	50½ lb		

TABLE B.

SHOWING THE LENGTHS OF PHALANGES AND METACARPALS IN MILLIMETRES OBTAINED FROM RADIOGRAMS (NORMAL FIGURES IN BRACKETS).

	Digit	Term. ph.	Mid. ph.	Prox. ph.	M'carpal	Sum total
Case 1	1st	14·0 (13·0)	20·0 (19·0)	34·0 (32·0)	52·0 (54·0)	120·0 (118·0)
	2nd	15·0 (14·0)	24·0 (23·0)	38·0 (37·0)	51·0 (52·0)	128·0 (126·0)
	3rd	15·0 (15·0)	23·0 (21·0)	36·0 (33·5)	45·5 (45·0)	119·5 (114·5)
	4th	12·0 (13·0)	16·0 (14·0)	27·0 (25·5)	42·0 (44·0)	97·0 (96·5)
	Thumb	20·0 (17·0)		25·5 (24·0)	36·0 (38·0)	81·5 (79·0)
Case 2	1st	9·0 (6·5)	11·5 (10·0)	22·0 (20·0)	29·5 (31·0)	72·0 (67·5)
	2nd	9·0 (7·5)	14·0 (13·0)	23·5 (23·0)	31·0 (29·0)	77·5 (72·5)
	3rd	9·0 (8·0)	13·5 (12·0)	23·0 (21·0)	28·0 (26·0)	73·5 (67·0)
	4th	8·0 (6·5)	10·0 (7·5)	18·5 (15·5)	23·5 (23·0)	60·0 (52·5)
	Thumb	12·0 (11·0)		16·0 (13·5)	21·0 (18·5)	49·0 (42·5)
Case 3	1st	13·5 (11·0)	18·5 (14·5)	32·0 (24·0)	51·0 (37·0)	115·0 (86·5)
	2nd	15·0 (10·0)	22·0 (17·5)	35·0 (27·0)	50·0 (36·0)	121·0 (90·5)
	3rd	15·0 (11·5)	21·0 (17·0)	32·0 (25·0)	44·0 (31·0)	112·0 (84·5)
	4th	12·0 (10·5)	14·5 (11·0)	24·5 (19·0)	40·0 (29·0)	91·0 (69·5)
	Thumb	17·5 (14·0)		23·0 (18·0)	36·0 (25·0)	76·5 (57·0)
Case 4	1st	14·5 (13·0)	19·0 (19·0)	32·5 (32·0)	52·0 (54·0)	118·0 (118·0)
	2nd	15·0 (14·0)	23·0 (23·0)	36·0 (37·0)	52·0 (52·0)	126·0 (126·0)
	3rd	16·0 (15·0)	22·0 (21·0)	33·0 (33·5)	46·0 (45·0)	117·0 (114·5)
	4th	14·0 (13·0)	16·5 (14·0)	26·0 (25·5)	42·0 (44·0)	98·5 (96·5)
	Thumb	20·0 (17·0)		25·0 (24·0)	35·5 (38·0)	80·5 (79·0)

TABLE C.

SHOWING THE RATIO OF THE SUM OF THE PHALANGES AND METACARPALS OF THE SECOND DIGIT TO TOTAL BODY LENGTHS.

Case	Ratio	Normal ratio
Case 1	1 to 10·04	1 to 11·4
Case 2	„ 10·03	„ 11·8
Case 3	„ 9·8	„ 10·1
Case 4	„ 10·2	„ 11·4

TABLE D.

SHOWING THE RATIOS OF THE SUM OF THE PHALANGES OF EACH DIGIT TO THE SUM OF THE PHALANGES PLUS CORRESPONDING METACARPAL BONES.

Case	1st digit	2nd digit	3rd digit	4th digit	Thumb
Case 1	1 to 1·76	1 to 1·66	1 to 1·61	1 to 1·76	1 to 1·79
Normal	1 to 1·84	1 to 1·71	1 to 1·66	1 to 1·83	1 to 1·92
Case 2	1 to 1·69	1 to 1·64	1 to 1·61	1 to 1·64	1 to 1·75
Normal	1 to 1·85	1 to 1·66	1 to 1·63	1 to 1·79	1 to 1·73
Case 3	1 to 1·8	1 to 1·68	1 to 1·64	1 to 1·8	1 to 1·88
Normal	1 to 1·74	1 to 1·65	1 to 1·58	1 to 1·71	1 to 1·78
Case 4	1 to 1·8	1 to 1·7	1 to 1·64	1 to 1·74	1 to 1·88
Normal	1 to 1·74	1 to 1·65	1 to 1·58	1 to 1·71	1 to 1·78

TABLE E.

SHOWING THE RATIO BETWEEN EACH PHALANX OF THE SECOND DIGIT TO THE CORRESPONDING METACARPAL.

Case	Terminal phalanx	Middle phalanx	Proximal phalanx
Case 1	1 to 3·40	1 to 2·12	1 to 1·30
Normal	1 to 3·70	1 to 2·26	1 to 1·40
Case 2	1 to 3·44	1 to 2·21	1 to 1·32
Normal	1 to 3·86	1 to 2·23	1 to 1·27
Case 3	1 to 3·33	1 to 2·22	1 to 1·43
Normal	1 to 3·60	1 to 2·09	1 to 1·33
Case 4	1 to 3·46	1 to 2·26	1 to 1·44
Normal	1 to 3·60	1 to 2·09	1 to 1·33

HEREDITARY ECTODERMAL DYSPLASIA

BY

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Of late years, a considerable amount of attention has been given in America and Germany to that class of case which has been variously termed 'combined defects of hair and teeth,' 'malformations simultanées du systéme dentaire et du systéme pileux,' and 'dystrophy of the hair and nails.' More recently the more comprehensive term 'congenital ectodermal defect' has been used, and still more recently, Weech[25], to whom I am indebted for much of the bibliography of this subject, has suggested 'hereditary ectodermal dysplasia' as the most suitable title.

The following is the case report of a child who shews what Goeckermann[9] and Mackee and Andrews [17] term 'high grade' or 'major' defect, or as Weech prefers to call it, the 'anhidrotic type of hereditary ectodermal dysplasia.'

Case Report.

A.B., aged 5 years 9 months, was first seen at an examination prior to attending school. He is the first of four children; two other children, aged three years and eight months respectively, are alive and well; one child died of pneumonia. Both mother and father are healthy and there is no evidence of similar anomalies in any other member of the family, excepting one aunt on the mother's side, who is said to have had a double set of teeth when a child, but it has not been possible to confirm this statement.

He was born at full term and, apart from an absence of hair on the scalp, was thought to be a normal child. He cut his first teeth, which occupy the normal position of the upper incisors, at 18 months; the four temporary first molars between two and three years, and the four permanent molars during the past three months. He began to walk at one year and ten months.

When three months old he was admitted to hospital suffering from convulsions of unknown origin. Apart from the high temperature (107·8°) nothing abnormal could be found in what appeared to be an otherwise healthy infant. After sponging with iced water the temperature fell to normal and the child was discharged well on the sixth day (18.7.23). He has had nine fits at intervals of a few weeks during the past summer; they all occurred between the months of May and October. He has also had attacks of epistaxis. The boy is said to have had no hair on the scalp for several months after birth, but a fine growth of hair can be seen in the photograph taken at the age of six months (Fig. 1). He never perspires even in the hottest weather, when he suffers extreme discomfort. During the summer months he frequently sleeps on the bare floor divested of all his clothes, and in the daytime often lets the cold water tap run over his head, from which procedure he appears to derive much benefit. In spite of the very imperfect dental development, he has little difficulty in mastication excepting with hard foods such as crusts.

Physical examination (17.12.28).—The patient was a slightly built child measuring 40 in. and weighing 33 lb. (normal for age 42 in. and 44 lb.). The most striking feature was the curious facies. The scalp, the skin of which was very dry and glossy, was covered with a sparse growth of very fair, floss-like hair. Large blue veins, which contrasted strikingly with the white, thin skin, coursed over the scalp but were especially well-marked in the fronto-parietal region, as shewn in Fig. 2. The eyebrows and eyelashes, although present were extremely scanty and there was no hair whatever to be seen on the rest of the body. The auricles were well formed and equal in size but stood out obliquely from the sides of the head. The bridge of the nose was considerably broadened and depressed and the skin here, being stretched to a greater extent than elsewhere on the face, had a bluish appearance. The nares were well developed and although there was some excoriation of the nostrils, there was no atrophic rhinitis or ozœna. The mucous membrane

of the mouth and pharynx appeared normal and there was an average amount of salivary secretion. The voice was not unduly shrill but the absence of teeth interfered considerably with articulation. The lips were thick and everted but the vermilion border was well defined. Both jaws were under-developed so that the face had a triangular appearance, having the forehead as base and the chin as apex. There were ten teeth present ; six in the upper and four in the lower jaw ; two occupied the position of the upper incisors ; there was one first temporary molar on either side in both jaws and posterior to each of these temporary teeth there was one, first permanent tooth. Using letters in alphabetical order for the temporary set and numbers for the permanent set his dental formula may be represented as follows :—

$$\frac{6D \quad 1\ 1 \quad D6}{6D \qquad\quad D6}$$

The molars were well formed and enamelled. The teeth in the incisor region, however were cone-shaped, the free end being sharply pointed, and were yellow in colour. The gums

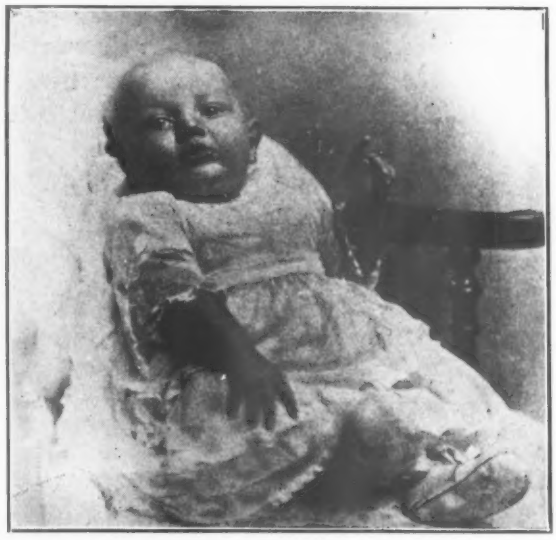


Fig. 1.—A.B., aged six months. There is a growth of fine hair on the scalp ; the thick, everted lips and the projecting ears are already noticeable.

where the teeth were absent were retracted and had a sharp narrow edge. The thin, parchment-like character of the skin, the large superficial scalp veins, the sunken nasal bridge and the under-developed jaws combined to give the child an old-mannish look. The bony prominences of the skull were well-marked, especially the supra-orbital ridges but the fontanelle was closed. The nipples were present but no glandular substance could be felt. Examination of the chest and abdomen revealed no abnormality. The child was forward mentally but seemed of an unduly sensitive nature. The genitalia were normal, and the nails on both hands and feet were well developed and smooth. There was no deficiency of lachrymal secretion but on no occasion was any sensible perspiration seen.

Investigations.—The Wassermann reaction was negative. The blood pressure, systolic 80, diastolic 45 mm. Hg. (normal 92·6 and 67·3). The colour index was rather low but examination of the blood revealed no gross abnormality. The sugar tolerance, urine and urea concentration tests were all normal, as were also the fundus and fields of vision and the skiagrams of the sella turcica and the long bones : no unerupted teeth were to be seen in the skiagrams. A piece of skin an inch long and a quarter of an inch wide was excised from the anterior chest wall in the anterior axillary line at about the level of the nipple. A series of a large number of sections was examined but no sweat or sebaceous glands or hair follicles could be found.

Review of the Literature.

It is surprising that although the first case of hereditary ectodermal dysplasia was reported in England in 1842 by Thurnam[23], the subject has received most attention elsewhere. It is also remarkable that although the anomaly is a congenital one it has but seldom been described during childhood. The literature abounds with cases of isolated ectodermal defects but there is one type of patient who deserves to be set in a class apart, for as Goeckermann says, 'In one group of cases of high grade congenital ectodermal defect . . . there is not only a congenital absence of teeth and a hypotrichosis, but also a total absence of sebaceous glands. This combination gives the cases a stamp which places them in a class by themselves.' The following cases come into this class and have already been reported in the literature :—

Table of Previously Reported Cases.

Author.	Date.	Sex.	Age.	Race.
1. Thurnam[23]	1842	male	58 years	English.
2. Thurnam	1842	male	13 ,,	English.
3. Williams[28]	1842	female	15 ,,	English.
4. Guilford[10]	1883	male	48 ,,	American.
5. Ascher[1]	1898	male	15 ,,	German.
6. Ascher	1898	male	21 ,,	German.
7. Tendlau[21]	1902	male	42 ,,	German.
8. Loewy & Wechselmann[16]	1911	male	—	German.
9. Christ[3]	1913	male	13 ,,	German.
10. Gibbs[7]	1915	male	7½ ,,	English.
11. Gibbs	1915	male	6½ ,,	English.
12. Strandberg[20]	1918	male	39 ,,	Swede.
13. Goeckermann[9] ...	1920	female	21 ,,	English.
14. MacKee & Andrews[17] ...	1924	male	14 ,,	Jew.
15. Weech[25]	1929	male	14 ,,	Jew.

The case which I have reported is therefore the sixteenth to be described, although it is probable that there are others which belong to this group but which, for lack of sufficient information cannot be included in this list. Hutchinson[12] shewed a boy aged three years at the Royal Medical and Chirurgical Society in 1886 whose description conforms very closely with those above, but as no note was made on the absence of perspiration, this patient has been omitted.

As stated previously, instances of various kinds of ectodermal dysplasia occur very frequently in the literature, and reports of dental anomalies of number, shape and date of eruption are especially common.

These dental variations may or may not be associated with abnormalities in the other ectodermal structures. Wieting[27] described a boy of twelve years who had been completely edentulous from birth, but who shewed no other peculiarity. Hopson[11] also has reported a similar case. In others the teeth and hair are affected simultaneously as was the case in Rushton's[18] patient,

an Armenian boy of sixteen, who had never had any teeth and whose hair was very soft and white, resembling wool. Darwin[5] also noted this tendency both in human beings and in animals. He speaks of Julia Pastrana, a Spanish dancer, who 'was a remarkably fine woman, but she had a thick masculine beard and a hairy forehead' and 'she had in both upper and lower jaw an irregular double set of teeth one row being placed within the other.' He also mentions that three hairless Egyptian dogs had many deficient teeth, and 'that the two orders of mammals namely the Edentata and Cetacea which are the most abnormal on their dermal covering are likewise the most abnormal either by deficiency or redundancy of teeth.'

Kjaer[15] described a man in whom the deciduous teeth had developed very imperfectly and the permanent teeth had never erupted, who was born without finger or toe nails. Eisenstadt[6] had three brothers suffering from a dystrophy of the hair and nails with no other ectodermal defect. Sufficient has been said to show that any combination of ectodermal defects may occur, but at the same time it seems desirable to differentiate from the others what Goeckermann calls 'high grade defect' and Weech 'the anhidrotic form of hereditary ectodermal dysplasia.'

Nosology.

Hitherto most of these cases have been described as examples of 'congenital ectodermal defect,' but as Weech says this is neither the most suitable nor the most comprehensive title. As this author points out 'hereditary' is to be preferred to 'congenital' for whereas the latter may connote either something existing at or dating from birth, 'hereditary' can only be applied to a condition which is capable of being transmitted from parent to offspring, and is therefore at the same time more comprehensive and precise. 'Dysplasia' is preferable to 'defect' for similar reasons. Weech's suggestion that this condition should be called 'the anhidrotic form of hereditary ectodermal dysplasia' has therefore been adopted throughout this article.

Symptomatolgy.

In reviewing the signs and symptoms attention should be drawn to the fact that although those recorded by Gibbs and the one reported here are the only examples of the condition in young children, several were seen at or about puberty, when the hypotrichosis which manifests itself later in the absence of beard, whiskers, pubic and axillary hair is not the prominent feature it is in adult life. This may partly account for their not being recognized during childhood.

Skin.—In all the cases described, the thin, smooth glossy skin has been a uniform feature and in all except the one described by Weech the skin has been fair, whereas in his boy 'the skin was everywhere rather dark.'

Histological examination of the skin was carried out by Thurnam, Tendlau, Goeckermann and in the present case, and although the skin was excised from such widely scattered areas as the arm, axilla, chest wall, epigastrium and pubis, the reports conform generally to the description given by Erasmus

Wilson of Thurnam's patient :—' The peculiarities of the portions of skin . . . are their whiteness, thinness and softness, and the tenuity of, and absence of pigment in the epiderma . . . The chief peculiarity, however, is . . . a state of extreme laxity and apparent atrophy of the derma, with a total absence of fat and the usual filling up material.' He goes on to say that ' the sudoriferous glands are not wanting but their ducts are unusually delicate and deficient

Fig. 2.—A.B., aged 5½ years. The dry, brittle, sparse hair, the large veins, the thick lips, the projecting ears and frontal eminences are well shown

in structure.' This last opinion was not confirmed by Bowman, who also examined the skin from the same patient and ' did not obtain satisfactory evidence of sweat or sebaceous glands or hair follicles.' Goeckermann reported a ' total absence of pilo-sebaceous and sudoriferous systems and their *anlagen*' in his sections. In the case recorded here none of these structures could be seen in the sections. From the patient's point of view this absence of sweat glands is of the utmost importance, since it is responsible for his extreme discomfort in hot weather.

Guilford[10] describes how, in order to keep cool in hot weather, his patient had to employ a boy to pour water over his clothing as soon as it became dry,

and if there happened to be any delay in the arrival of the water he became weak and would be nearly thrown into a spasm by the intense internal heat. Tendlau's own description is :—' Wurde die Hitze zu stark, so stellte sich heftigen Blutandrang nach dem Kopfe ein, und er musste dann die Arbeit aussetzen, ja oftmals brach er fast bewusstlos bei derselben zuzammen.' I have described how my patient when only three months old had an attack of hyperpyrexia accompanied by fits and that during the summer he still has the fits. Tendlau carried out certain experiments on the excretory function of the skin in his patient and found that pilocarpine had no sudorific effect. He also noted that five minutes after drinking hot milk, the patient's temperature rose from 36.9° to 37.1° C, and that on standing in the sun for 20 minutes when the air temperature was 32° C., the patient's temperature rose from 36.7° to 38.8° C., the rise being accompanied by severe headache and discomfort. Loewy and Wechselmann made observations on the evaporation and excretion of water from the skin in their patients.

Fig. 3.—A.B. Showing the sharply pointed teeth in the upper incisor position.

Skin eruptions.—Papular lesions on the face have been described by several writers. Loewy and Wechselmann and Goeckermann diagnosed them as milium ; Christ thought it similar to xeroderma pigmentosa ; Strandberg thought it was of pilo-sebaceous origin, while MacKee and Andrews, who examined them histologically, state that ' the lesions appeared to be the result of large, superficially placed, degenerated sebaceous glands, together with hyperkeratosis, dilated follicular orifices, and surrounding acanthosis.' Epidermolysis bullosa has been noted in association with certain congenital defects, but not as yet in the anhidrotic type.

Teeth.—Abnormal dentition is a constant feature in these patients and affects both temporary and permanent sets, in number, form and date of eruption. Some are edentulous as was Guilford's patient, but more usually a few of each set appear. In several, delayed eruption has been noted and deformed teeth are common, the ones so affected being those which occupy the upper incisor position, although it is difficult to tell whether they are incisors or canines, as they occupy the position of the former, while resembling the latter more closely in shape. These teeth are often yellow and cone shaped ; sometimes the free end is sharply pointed and tusk-like, or as MacKee and Andrews say, 'gimlet-like.' The molars, though often deficient in number, are normal in form.

Hair.—The hair on the scalp is fine, fair, dry and sparse. Some patients had no hair for several months after birth ; others had a feeble growth which did not improve as the child grew older. The sparseness is very marked in all cases, so that the dry, glossy skin shines through between the hairs. It is interesting to note that no case of alopecia areata has been recorded among these patients, although the mother of Hutchinson's patient, who as stated elsewhere should probably come into this group, had been compelled from the age of six to wear a wig on account of a complete alopecia areata.

The lanugo hair on the body is generally absent, but the axillary and the pubic hair varies ; some patients have no growth whereas in others it is normal. MacKee and Andrews and Strandberg noted that the pubic hair grew in the female distribution. Eyelashes and eyebrows, especially the outer third of the latter, are either absent or scanty. It is curious, as Weech points out, that even when there has been no beard or whiskers, the patient has usually grown a moustache.

Nails.—Dysplasia of the nails is nothing like so frequent as are abnormalities in the hair and teeth. Goeckermann mentions that the nails had longitudinal furrows ; MacKee and Andrews that they had free lateral margins, which were flush with the skin instead of being imbedded, and Hutchinson's patient's were spoon-shaped, but in most cases they are normal.

Mammary glands.—Absence of the nipples and mammary glands were noted by Tendlau. Ascher's patient had flat nipples and breasts in which no glandular substance could be felt. Hutchinson wrote that his boy had no nipples, their sites being occupied by little patches of scar tissue and nothing like a mammary gland could be traced.

Lachrymal glands.—Thurnam's two patients are the only ones on record in which the lachrymal secretion was absent. His first patient had never been known to shed tears and 'the painful emotions generally relieved in this way had in him an unusually distressing appearance.' The lachrymal buds are of ectodermal origin and form at the third month of intrauterine life, *i.e.*, at the same time as the teeth are laid down, and it is strange that absence or diminution of this secretion has not been noticed in any other patient.

Nose, mouth and throat.—One of the main features, and one which plays an important part in the characteristic facies of these patients, is the broad, sunken nasal bridge or saddle nose, which is often so marked as to suggest a luetic origin. It is probable, however, that although it is not a syphilitic stigma, its mode of production is similar, and that it is due to an osteo-perichondritis, since there is almost always a history of nasal trouble in early life. Goeckermann's patient had had trouble since he was nine months old, and Weech states that his first patient had 'dry snuffles' at four months. In adult life there is frequently an atrophic rhinitis. The depression of the nasal bridge is accentuated by the projection of the frontal bones and more especially the supra-orbital ridges. Atrophic changes in the pharyngeal and laryngeal mucous membranes were marked in Tendlau's patient, whose voice was shrill and hoarse. The mucous membrane of the mouth and the salivary secretion are usually normal. MacKee and Andrews and Goeckermann described poor definition of the vermilion border of the lips, but this is not constant. Although Guilford's man had no sense of smell and that of taste was poor, the special senses are often unaffected, and when they are, it probably is the result of changes in the mucosæ.

The lips are everted, thick and muscular. This has been attributed to their excessive use in mastication rendered necessary by the absence of teeth, but in the photograph of my patient (Fig. 1) taken at the age of six months, this eversion is already well marked. Weech says that the epithelium on his patient's lips was thickened at nine weeks, and MacKee and Andrews noticed that the vertical lines on the lips were more pronounced than normally.

Ears and eyes.—The auricles of Ascher's first patient stood out obliquely from the sides of the head, and were unequal in size, the right being smaller than the left, while MacKee and Andrews noticed the lobes of the ears were small and attached to the cheeks.

Darwin asserts that the organs of sight and hearing are generally admitted to be homologous both with each other and with the various dermal appendages; hence these parts are liable to be abnormally affected in conjunction. Moreover, White Cowper[1] mentions that in all cases of double microphthalmia brought to his notice, he met at the same time with defective development of the dental system. On the other hand in all the subjects of the anhidrotic form of ectodermal dysplasia where a note of the special senses has been made, hearing and vision appear to be normal.

Nervous system.—It is interesting that although the nervous system is ectodermal in origin, gross malformations of this system have not been recorded. Tendlau, Loewy and Wechselmann and Christ mention that their patients were of feeble intelligence; in other instances, there were insane members in the family (Thurnam), but the greater number have been of average intelligence. My patient, indeed, although he has never attended school, reads better than many of the same age and is quick at mental arithmetic. Reflexes, sensation and motor power were normal in all those who have been examined.

Osseous system.—Although the osseous system is of mesodermal and not of ectodermal origin, certain peculiarities of the skull bones have been constantly present. Thurnam's patient, the only one on whom an autopsy has been held, shewed the dura mater firmly adherent to the calvarium which was very thick. All the writers mention the prominent supraorbital ridges and occipital and other eminences of the skull. There was no increase in the density of the skeletal bones or any epiphyseal changes in the boy here described, but the abnormally high blood calcium may have some, as yet unknown, significance.

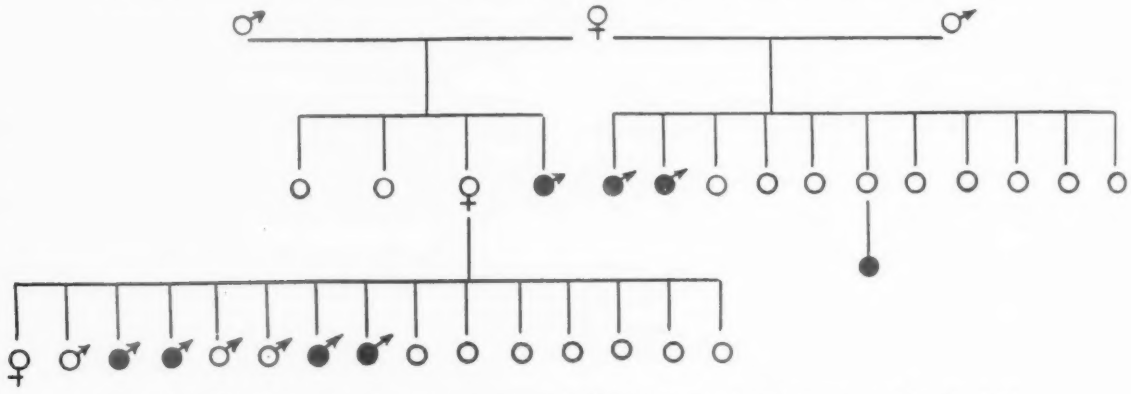
Ætiology.

Congenital Syphilis.—The facial aspect has often led to a tentative diagnosis of congenital syphilis, and indeed the pallor, large head, the eminences of which are very pronounced, the large superficial veins, saddle shaped nose, and sparse dry hair may easily suggest this diagnosis, which in some patients would appear to be still further supported by a history of papular eruption and rhagades on the face, a desquamation of the palms and soles, and of snuffles. The Wassermann reaction has never been found positive and the teeth, although malformed, bear no resemblance to Hutchinson's teeth. It has been pointed out that the ectodermal structures are developing during the third month of intra-uterine life, and, as Goeckermann says, it is very unlikely tha tif the spirochæta pallida were the causative agent its injurious influence would be exerted particularly at that time and then be suddenly removed ; nor is it likely that it would at that early date have a selective action on ectodermal structures.

Endocrine dyscrasia.—Our knowledge of the role of the hormones during intra-uterine life is as yet very imperfect, but some aspects of these cases suggest an endocrine dyscrasia, and this hypothesis cannot therefore be wholly disregarded. Thurnam's patient had a bronchocele ; the basal metabolic rate in Weech's patient was 10 per cent. below the normal and was associated with a small sella turcica ; MacKee and Andrews and Strandberg noticed that the pubic hair grew in the female distribution. Barrett[2] found an increased sugar tolerance in a patient suffering from a dystrophy of the hair and nails, and Wheelon[26] described four patients, three of whom were females, in whom the upper lateral incisors were deformed or absent : the females shewed marked signs of pituitary insufficiency such as obesity, low basal metabolic rate and amenorrhœa, while the male exhibited signs of hyperfunction of the gonads. Moreover, Keith[14] maintains that ' we have evidence that the growth of the canine teeth can be regulated by internal secretions or hormones,' and that ' the growth of the jaws is also influenced, during normal development, by secretions or substances thrown into the blood by such glands as the pituitary and thyroid.' Vichot[24] also thinks that an abnormal condition of the glands of internal secretions is one of the primary factors in dental regression and adds that ' les facteurs primaires créent les variations ; l'hérédité semble les fixer.' That deficiency of the thyroid secretion leads to excessive dryness of the skin and hair is well known and that many of the glands affect the deposition of fat, the absence of which is such a marked feature in these subjects, is also

recognized, so that although it is difficult to attribute hereditary ectodermal dysplasia entirely to an endocrine dyscrasia, it is possible that it may play some part in its production.

Heredity.—The majority of these cases have shewn marked hereditary tendencies. The most complete family history illustrating the transmission of hereditary ectodermal dysplasia is that of the Kitzings, of whom two members were described by Ascher and one other by Loewy and Wechselmann. From the data given by these authors Weech has constructed the following pedigree chart. This chart shews that eight members of the family were affected, seven of whom were males and the sex of the other is not stated. Thurnam's



second patient was a cousin-german of the first, and Thurnam adds that the maternal grandmother had very delicate skin and a very limited amount of perspiration, but no peculiarity of the hair or teeth. Guilford's patient illustrates the tendency to transmit associated dysplasia of the hair and teeth although the patient himself was the only member of his family who did not perspire; his maternal grandmother had no teeth or hair; her daughter, the mother of the patient, was normal but her brother was edentulous from birth; the patient was one of twenty-one children, one of the later ones, and although he was the only one who was completely edentulous, some of his brothers had never erupted certain teeth; the patient was the father of eight children, the two youngest of whom, aged fourteen and sixteen years respectively, had many teeth absent; it is not stated whether the patient's uncle, who was hairless and edentulous too, perspired or not.

A similar history was given by the mother of Gibb's two boys. The father was normal and none of his relatives had any dental anomalies; the mother, however, was the second of eight children, and although her parents were normal, two brothers had very pointed teeth, and several of her sister's children (sex not stated) shewed abnormal dentition. Christ's patient had a younger brother and a first cousin on his mother's side who were similarly affected. On the other hand no pertinent family histories could be obtained by Strandberg, MacKee and Andrews, Goeckermann, Weech (first case) or myself.

One of the most striking facts which emerges from a study of these data is that, excepting the patients recorded by Williams and Guilford, all have been males. Moreover, there is "a report by Thadani[22] of a type of man

occurring in the Hindu Amil community of Hyderabad Sind, a town in India, who is 'characterized by an absence of teeth, a bald head and by extreme sensitiveness to heat.' Although meagre, this description is probably sufficient to identify them as persons afflicted with the anhidrotic form of ectodermal dysplasia. Thadani's publication was in the nature of a preliminary report. Actual pedigrees were not given, but the author stated that the inheritance has been strictly sex-linked " (Weech). The chart of the Kitzing family shews especially clearly that the anomaly was here also transmitted by the female and inherited by the male.

It is interesting to contrast with these facts Jacobsen's conclusions on the inheritance of dystrophy of the hair and nails of which he traced sixty-four members in five generations of one family. From his study he decided that the transmission was Mendelian and not sex-linked.

It is impossible with the scanty material available to make generalizations and it is especially difficult to explain the occurrence of what would appear to be a sex-linked character in the female. Weech believes that this condition must have its origin in a genetic mutation, and that this mutation may in the beginning occur in either sex, but thereafter the transmission would be sex-linked and the anomalies would appear only in the male. In support of this hypothesis he points out that in neither of the female patients described in the literature is there a record of antecedents affected, and that the history in Guilford's case, of an affected woman transmitting the characteristics through a non-affected daughter to an affected son, may be explained in the same way.

Diagnosis.

In discussing the symptomatology it has been mentioned that these patients bear many superficial resemblances to the subjects of congenital syphilis. The absence of visceral involvement, eye lesions, bone or joint affections, the consistently negative Wassermann reaction and the non-luetic family history, should be sufficient to prevent the erroneous diagnosis of this disease.

Another condition which may suggest itself is progeria. Weech mentions that two competent observers made this diagnosis of his patient and the same suggestion was made with regard to my patient[19], but there are several features which distinguish it from that extraordinary condition described by Hastings Gilford[8], indeed the similarity is entirely based on the aged appearance produced by the sparse white hair and the under-development of the edentulous jaws. There are no signs of arteriosclerosis or renal disease, and although the skin is dry it has not the wrinkled appearance of advanced senility found in progeria. The prognosis in the two conditions is very different, for whereas the subject of progeria usually dies about puberty, those with hereditary ectodermal dysplasia often lead active lives to a good age.

Yet another condition from which this must be differentiated is xeroderma. These patients certainly do suffer from a xeroderma using the word in its etymological sense, but it differs from the more limited conception of the dermatologist in that it shews a sex-linked inheritance, an absence of sweat

glands and an association with dental and other ectodermal anomalies. Renal and other forms of infantilism may suggest themselves but a careful general examination should render their exclusion simple, for although these patients are slightly built and often considerably under the normal weight owing to the paucity of subcutaneous fat, there is no delay in the onset of puberty, and sexual function is normal, nor is there any evidence of renal disease.

SUMMARY.

A case of hereditary ectodermal dysplasia is described and a review of the literature, in which fifteen other cases have been recorded, has been made.

Numerous instances of various forms of ectodermal dysplasia have been hitherto reported but the cases described in this communication form a clearly defined class which is best styled 'the anhidrotic form of hereditary ectodermal dysplasia.' Reasons for preferring this title, which was suggested by Weech, to the older one of 'congenital ectodermal defect' are given.

The symptomatology is described and the diagnosis from congenital syphilis, progeria, xeroderma, renal and other forms of infantilism discussed. Syphilis is not an ætiological factor and although endocrine dyscrasia may play some part in creating these, the most striking feature is the inheritance which appears to be sex-linked.

I am greatly indebted to Dr. C. K. J. Hamilton, Dr. Montague Maizels and Mr. W. D. Southern for their help and advice in the preparation of this paper.

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A CASE OF PROBABLE ANTENATAL TUBERCULOUS INFECTION.

BY

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The following case of miliary tuberculosis in an infant of six weeks old presents several unusual features of interest. The possibility of antenatal infection from the placenta is now regarded as established, though of rare occurrence, and in the case here reported seems the most reasonable explanation of very advanced lesions in so young a subject.

Clinical history.—The child, a male, was born at home on December 20th, 1928, at full term and weighed 7 lb. Delivery was normal and the doctor in attendance noticed nothing unusual about the child or the placenta. The child was wholly breast fed and developed satisfactorily until 4 weeks old, when he began to fall off, with diarrhœa, loss of weight and inability to take his food, and at this time a patent food was substituted for the breast milk. One week later, on January 26th, 1929, he was admitted to hospital where he went steadily from bad to worse, being unable to take nourishment and running a temperature up to 102°F. He died on January 31st and an autopsy was performed on the following day.

Summary of post-mortem examination.—The peritoneal cavity contained a few ounces of clear straw-coloured fluid. The liver showed a generalized tuberculous lesion in the form of rather irregular crude and miliary tubercles, 1 to 4 mm. in diameter, scattered throughout its substance. The cœliac glands lying between the head of the pancreas and the portal fissure showed an advanced caseating tuberculous lesion with central cavitation. The spleen contained innumerable crude and miliary tubercles up to 4 mm. in diameter. The kidneys contained a few small scattered tubercles definitely of crude caseous type, the largest being 2–3 mm. in diameter. The mesenteric glands showed a few small caseous tuberculous foci, much smaller and more recent than those in the cœliac group. The lungs contained numerous crude yellow tubercles up to 7 mm. in diameter, together with many fine miliary tubercles. The bronchial glands were the seat of early caseating tuberculosis. In addition there were scattered miliary tubercles in the adrenals, the gastric and intestinal mucosæ, the pleuræ and the myocardium. The most advanced lesion was certainly that of the cœliac group of glands.

Histological examination.—The liver is uniformly studded with tubercles in which may be distinguished two types of response, occasionally associated in the same tubercle but most frequently occurring separately. (1) There is a definite and typical follicle with epithelioid cells, slight necrosis, formation of giant cells of small size and a little peripheral lymphocytic infiltration. These tubercles stain pink with hæmalum and eosin, and contain only an occasional tubercle bacillus. (2) Secondly, there is a lesion which is essentially necrotic with very notable basic staining on account of the abundant pyknotic nuclear material present. In this form tubercle bacilli are present in myriads but there is little cellular reaction and no giant cells are seen. There is considerable lymphocytic infiltration of the portal tracts. The lobular arrangement of the hepatic cells is disturbed and they show fatty degeneration.

The mass of cœliac glands is largely caseous and contains many tubercle bacilli. The adrenals are sparsely studded with miliary tubercles in which necrosis is the outstanding feature with notable absence of lymphocytic, endothelial cell, and giant cell reaction. Tubercle bacilli are present in large numbers. The spleen contains numerous large necrotic tubercles. They present the same general characteristics as those in the adrenals. Tubercle bacilli are present in large numbers. The lungs show aggregated tubercles, of varying size, having the same characteristics as those in adrenals and spleen. Many of the alveoli are filled with caseous plugs. Tubercle bacilli are more numerous in this than in any other organ.

It is fairly certain that the two types of lesion in the liver are of different ages (1) being of some weeks standing, and (2) probably only a few days to a week or so. The lesions observed in the other organs correspond in general to those of the second type in the predominance of necrosis with little reaction and in the presence of enormous numbers of bacilli.

Family history.—All four grandparents are healthy and living. The mother, aged 25, has been married for two years and this was the first child. She is of healthy appearance and gives no medical history of note. Of her own family, father, mother, two brothers and a sister are all healthy and there have been no deaths. The physical examination, including X-ray examination of the chest and sputum tests, is entirely negative..

The father, aged 28, a tram driver, is of healthy appearance and has also no medical history of note. His father, mother, four brothers and sisters are all healthy. Three died in infancy of unknown causes. On examination, he is fairly well developed. There is some flattening of the left chest and slight impairment of resonance at the apex, without adventitious signs. The sputum contains no tubercle bacilli. An X-ray of the chest shows increased root shadows on the left side but no sign of active phthisis.

Discussion.

The argument for an antenatal infection is based on the early age at death and the anatomical characters and distribution of the lesions.

Age. It seems very unlikely that lesions so advanced as those in the liver and cœliac glands could have originated within six weeks of death.

Anatomical distribution. The most striking feature of the morbid anatomy is the extent to which the cœliac group of glands was affected, whereas in the mediastinal and mesenteric groups the process was both slighter and more recent. This suggests a direct infection from the placenta and as, in the absence of lymphatics in the umbilical cord, the infection must have been blood-borne, evidence of antecedent infection of the liver would be expected. Here it is to be found in the first of the two types of lesion above described, well formed tubercles with giant cells and abundant epitheliod cells. It is assumed that these lesions were produced by lodgement in the liver of tubercle bacilli passing in the umbilical veins from the placenta, that the portal and cœliac glands were infected by drainage from the liver and that miliary dissemination took place therefrom, probably via the thoracic duct, with production of the second type of lesion. In this connection the numbers of bacilli in the two types is worthy of comment, only one or two being seen in the older original tubercles and enormous numbers in the recent lesions. The fact that the placenta was not obviously diseased is not surprising, as reference to Warthin's[2] account of placental tuberculosis shows that frequently there is no naked-eye evidence and that histologically tubercles are sometimes found in the walls of chorionic vessels thus providing ready access to the umbilical blood-stream.

To explain antenatal infection it seems necessary to assume either (*a*) a general blood infection of the mother, (*b*) genital tract infection of the mother, or (*c*) genital tract infection of the father, though this must be a rare cause.

Actually, physical examination of the parents was strikingly negative, they both feel perfectly well and the whole affair is an inexplicable mystery to them. Certainly a general tuberculous infection of either, and genital tract infection of the father can be excluded, and the only possibility that remains

is that the mother suffers from some latent tuberculosis of the genital tract. And if evidence of antenatal infection is lacking, so is that of post-natal, for the home surroundings were reasonably healthy, the child never came in contact with a recognized tuberculous subject, and moreover, was entirely breast-fed until the onset of symptoms.

In connection with this case it is interesting to refer to reviews of supposed cases of congenital tuberculosis. In 1904 Warthin and Cowie[3] reviewed the cases reported up till then, the list including five undoubted cases and thirty-one probable or doubtful cases. In none of these was the mother specifically stated to be healthy.

Since then a very large number of cases has been reported and Calmette and others[1] in 1926, following up the histories of 100 pregnant tuberculous women, found abortion, still-birth or death in infancy in twenty-one : autopsy was performed on nine of these infants and in only three were tubercle bacilli demonstrated. In this and similar investigations only the children of frankly tuberculous mothers have been examined, and the present case is especially interesting in that it was accidentally brought to light.

Summary.

The chief points of interest in the case are as follows :—

1. The likelihood, from the foregoing considerations, of its being one of antenatal infection.
2. The complete absence of signs or symptoms of tuberculosis in the mother.
3. The apparent healthiness of the child at birth.
4. The evidence of two stages in the infection of the infant, a definitely older lesion in the liver with well-marked cellular reaction, presumably antenatal and of placental origin, and a very recent general miliary tuberculosis in which the lesions are necrotic in type and, in contradistinction to the others, contain tubercle bacilli in enormous numbers.

I am much indebted to Dr. Vining, under whose care the child was admitted to the Leeds General Infirmary, for permission to publish the case.

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DISPLACEMENT OF THE HEART IN PNEUMONIA IN CHILDHOOD.

BY

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In cases of collapse of the lung it is well-known that the heart deviates towards the side of the lesion, and, since its description by Pasteur in 1890, this displacement of the heart has been generally regarded as the principal physical sign of the condition. That a similar phenomenon frequently occurs during the course of pneumonia in childhood is, however, not widely known, if one may judge by the scanty literature on the subject and the absence of references to it in textbooks. On this account it would seem to be of interest to report the following cases in which this condition was observed, and to deal in some detail with the subject.

Three of the cases mentioned below have already been shown, and their condition two years ago, briefly reported in the *Proceedings of the Royal Society of Medicine*[1].

In 1922 Thoenes[2] reported a series of 11 cases of pneumonia in infants, in all of which he noted displacement of the mediastinal contents, and especially of the heart, towards the affected lung. As the pneumonia resolved, the heart went back, though slowly, to its normal position.

The next paper to appear on this subject was that of Wallgren[3], who reported 8 cases occurring both in infants and in older children, in which similar findings were noted. There appears to be no further publication in this connection until 1927, when Griffith[4] reported displacement of the heart taking place during the course of pneumonia in 16 out of 40 cases, and gave details of the cases of 7 infants in which this occurred. It is difficult to be certain of the type of pneumonia present in the cases reported, since the symptoms, physical signs, and course of the disease are not all clearly defined. In Thoenes's series, however, lobar pneumonia and broncho-pneumonia would appear to have occurred in approximately equal numbers, while in Wallgren's and Griffith's cases, lobar pneumonia predominated. Griffith in fact states definitely that the majority of his cases conformed to the type of croupous pneumonia without discoverable signs of atelectasis.

The question arises as to the causation of this cardiac displacement, and it is this which is probably of chief interest. Two factors are apparently at work: on the one hand a traction of the mediastinal contents towards the affected side as the result of the shrinkage and partial collapse of the diseased lung; and on the other hand, a push exerted from the sound side by the unaffected lung, distended by compensatory emphysema. In post-mortem examinations of cases dying of broncho-pneumonia, it is usual to find in the affected portions of lung, areas of collapse coexistent with areas of consolidation. Such a condition occurring in mass in the affected lung,

together with emphysema—probably compensatory—on the opposite side, would seem to explain adequately both the deviation of the heart and the direction of its displacement. Wallgren and Griffith regard emphysema and distention of the sound lung as the chief factors concerned. Thoenes lays stress on collapse of the affected lung, and gives two autopsy records which support these views.

Coryllos and Birnbaum[5] have thrown further light on this subject, and in their interesting paper recently published, bring forward evidence showing that pneumonia is an atelectasis associated with infection. Collapse of the lung, either of a whole lobe, or, in the case of broncho-pneumonia, a patchy atelectasis, would in their opinion be the cause of displacement of the mediastinal contents.

From a consideration of our five cases detailed below, together with those already referred to in the literature, it appears that in all probability both factors come into play in the causation of this phenomenon.

Clinical Reports.

Case I. M.G., age 1 month. Admitted to Hospital with typical symptoms of pneumonia. History of two days' cough, fever and embarrassed respiration.

23/2/28. Crepitations and rhonchi heard over both lungs.

3/3/28. Slightly diminished air entry and impaired percussion note, right lower lobe.

6/3/28. X-ray photograph shows the heart and trachea both lying to the right, with a definite increase in density of the right upper lobe (Fig. 1).

8/3/28. Impaired percussion note and diminished breath sounds in right upper lobe, with crepitations throughout right lung. Area of cardiac dullness not defined. Apex beat appears to lie below the 4th space beneath the sternum.

13/3/28. X-ray photograph shows upper lobe of right lung clearing, with the heart slightly more normal in position, but still well to the right.

30/3/28. No definite physical signs now in chest, and heart appears in normal position on clinical examination. X-ray picture taken at this time shows heart and trachea returning towards the left, and the apex of right lung clear. Child's general condition good.

6/6/28. Child doing well and gaining weight satisfactorily. No abnormal physical signs. X-ray shows heart practically normal in position; slight degree of mottling at apex.

Case II. E.A., age 4 months. Said to have had bronchitis for three weeks. Three days before admission had a convulsion, and on the day of admission a further convulsion with feverishness and embarrassed respiration.

2/2/28. On admission respiration rapid; rhonchi heard throughout the left lung with harsh breath sounds. Over right lung, breath sounds high pitched, percussion note impaired, and crepitations and rhonchi throughout all lobes: the area of cardiac dullness cannot be defined, since there appears to be some emphysema over left side of chest, but the heart sounds are heard rather better to the right of the sternum. Spleen palpable.

27/2/28. X-ray photograph shows heart and trachea displaced to the right with areas of opacity in the middle and lower lobes of the right lung.

1/3/28. Respiration becoming normal. Left lung clear except for a few crepitations at the base. In the right lung physical signs remain the same, although the percussion note posteriorly is now normal. Heart sounds heard more clearly to the left than previously.

5/3/28. X-ray shows heart and trachea in approximately the same position, though the lung itself is clearing. The chief area of opacity is well seen on the screen, but is not so obvious in the X-ray film, being overlapped by the heart shadow.

20/3/28. Percussion note impaired and crepitations present at right base. Heart still appears to the right. X-ray picture shows lung clear and heart returning, although not yet in normal position.

27/3/28. Crepitations still present at the right base. Clinically heart appears to be normal in position now.

17/4/28. Child seems very well. Physical signs at right base unchanged. X-ray picture shows right lung clear, and the heart and trachea now practically normal in position.

22/5/28. Some cough and bronchitis present. Crepitations also heard at right base.

5/6/28. Occasional crepitations right base; no other physical signs. No cough now, and child seems well. X-ray shows the lungs to be clear, but neither heart nor trachea has returned completely to its normal position.

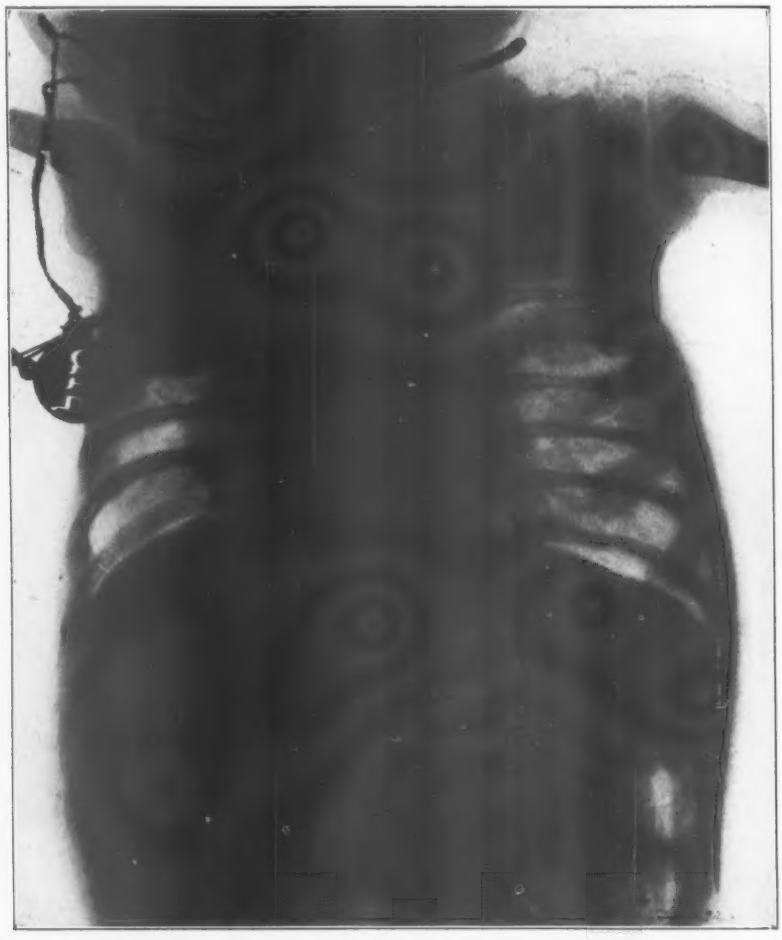

FIG. 1. Case I., M.G. 6/3/28. The heart is seen to lie almost entirely in the right side of the chest; the apex of the right lung is opaque.

3/7/28. Child well and gaining weight very satisfactorily. Chest clear of physical signs.

18/8/28. Recurrence of cough. Rhonchi throughout both lungs, and some crepitations heard at the left base.

25/9/28. No cough now. Infant seems well though the chest is said to be "rattley" at times. She has cut no teeth yet, though her weight is up to normal. Excepting a few scattered rhonchi, there are no physical signs in the chest. X-ray shows that there is still a small area of increased density in the right lower lobe to right of heart. Heart appears normal in position now.

22/11/28. Crawling and starting to walk. Still no teeth (14 months old now). Apart from diminished breath sounds and a few crepitations heard over the right lower lobe on deep breathing, there is nothing abnormal to be noted in the chest now.

Case III. L.M., age 10 months. Three days' history of vomiting and off food.

10/10/27. On admission, infant very cyanosed, with embarrassed respiration and marked stridor. Apparently much mucus in the trachea : throat swab negative. Coarse crepitations at both bases and rhonchi throughout both lungs. Heart apparently normal in position. Spleen palpable.

25/10/27. Dullness and diminished breath sounds right base. No area of cardiac dullness defined. Heart sounds heard most loudly just medial to right nipple.

26/10/27. X-ray photograph shows no cardiac shadow in left side of the chest, but an opacity throughout right side, with the trachea pulled over to the right. The picture was taken under difficulties, oxygen being administered by nasal catheter. (The question of a foreign body in the bronchus was considered at this time.)

28/10/27. No change radiologically (Fig. 2).

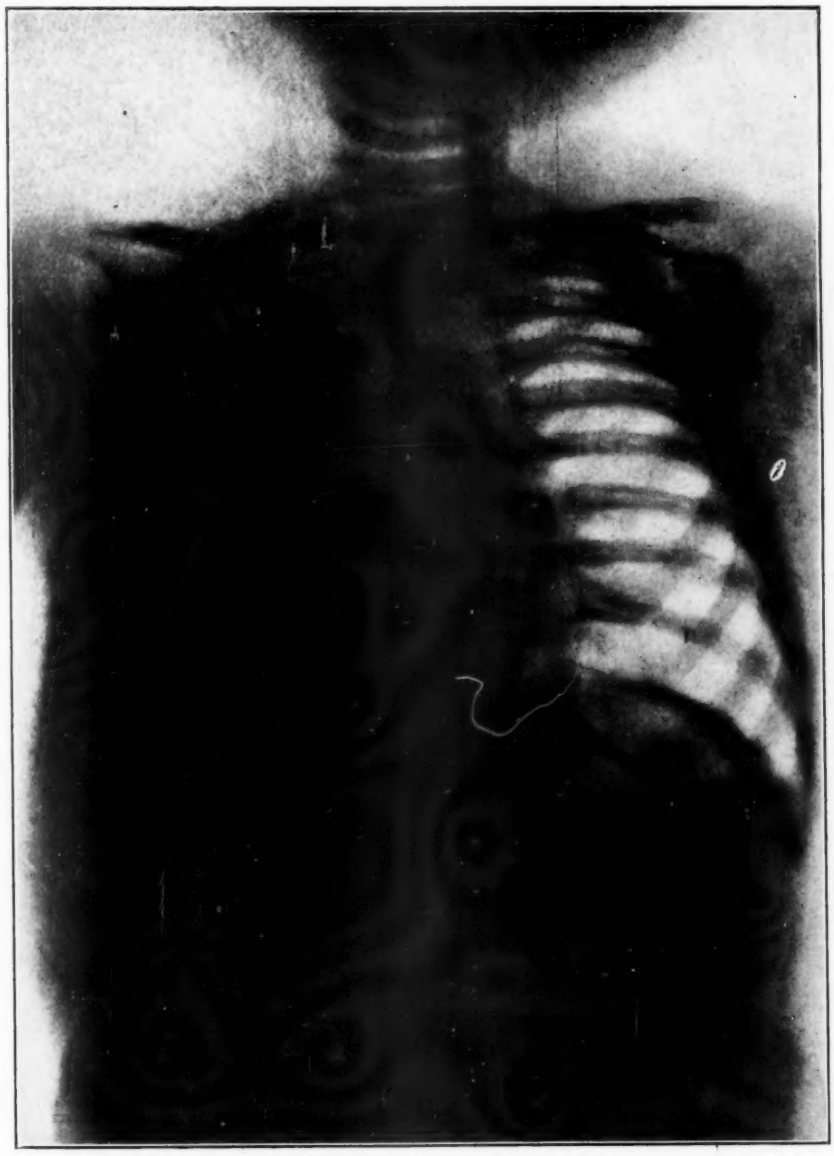

FIG. 2. Case III., L.M. 28/10/27. The heart lies completely in the right side of the chest, which is opaque, so that no cardiac shadow is seen. The trachea is seen well to the right of the mid-line.

31/10/27. Dullness, bronchial breath sounds and rhonchi throughout right lung, with deficient movement of right side of chest.

3/11/27. Percussion note still impaired. Breath sounds high pitched over right lower and middle lobes. Heart displaced to right and respiration rate still raised, but temperature now normal.

From now onwards the right lung cleared, and the heart gradually returned to the normal position as shown by physical signs, and the following X-ray pictures:

5/11/27. X-ray shows upper right chest almost clear, but the right base remains opaque. The trachea is seen well to the right side, but the apex of the heart can be noted to the left of the spine, showing that it is returning to its normal position; the right border of the mediastinal shadow can be seen (Fig. 3).

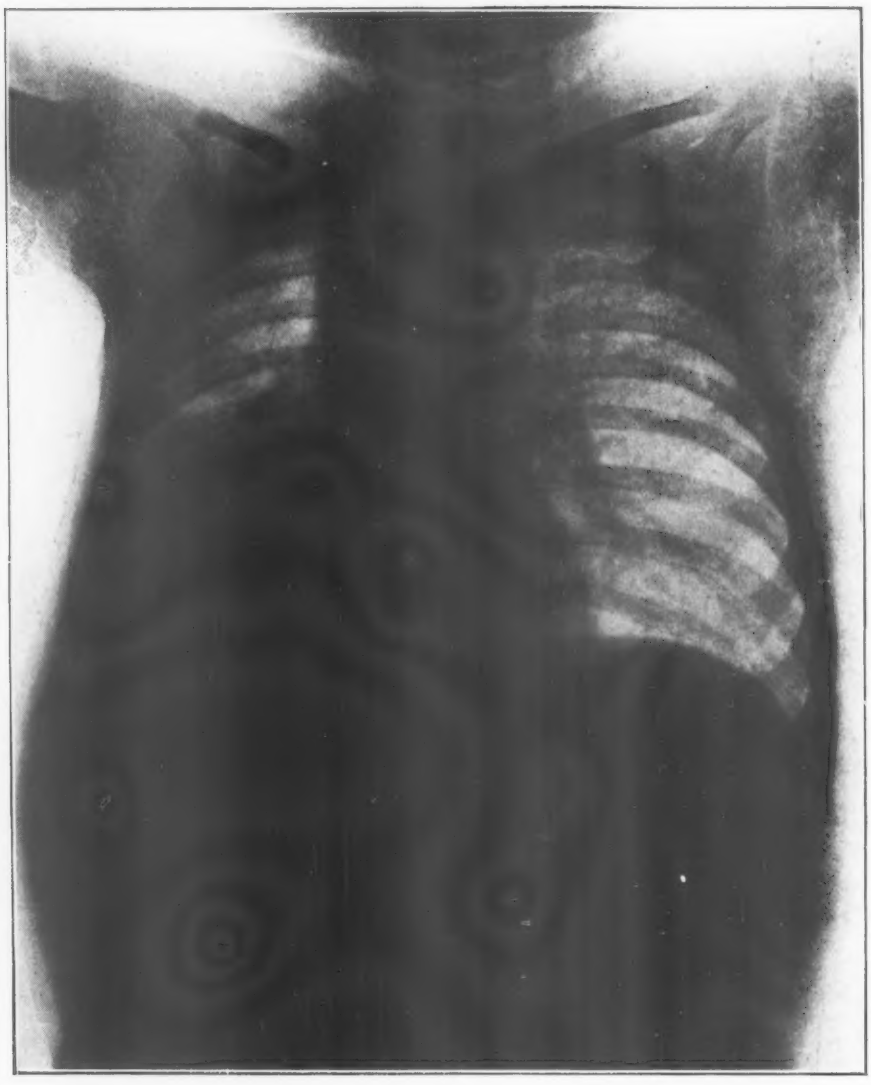

FIG. 3. Case III., L.M. 5/11/27. The right upper chest is almost clear; the apex of the heart can be seen appearing to the left of the spine, but there is still marked cardiac displacement towards the side of the lesion.

12/11/27. X-ray still shows area of density at right lower lobe, probably a patch of unresolved pneumonic consolidation. The heart is returning to the normal position.

1/12/27. X-ray now shows unresolved area much improved.

17/12/27. Physical examination shows no physical signs whatever, and the heart appears normal in position. X-ray shows the heart and trachea to be still displaced and the unresolving area to have increased in size (Fig. 4).

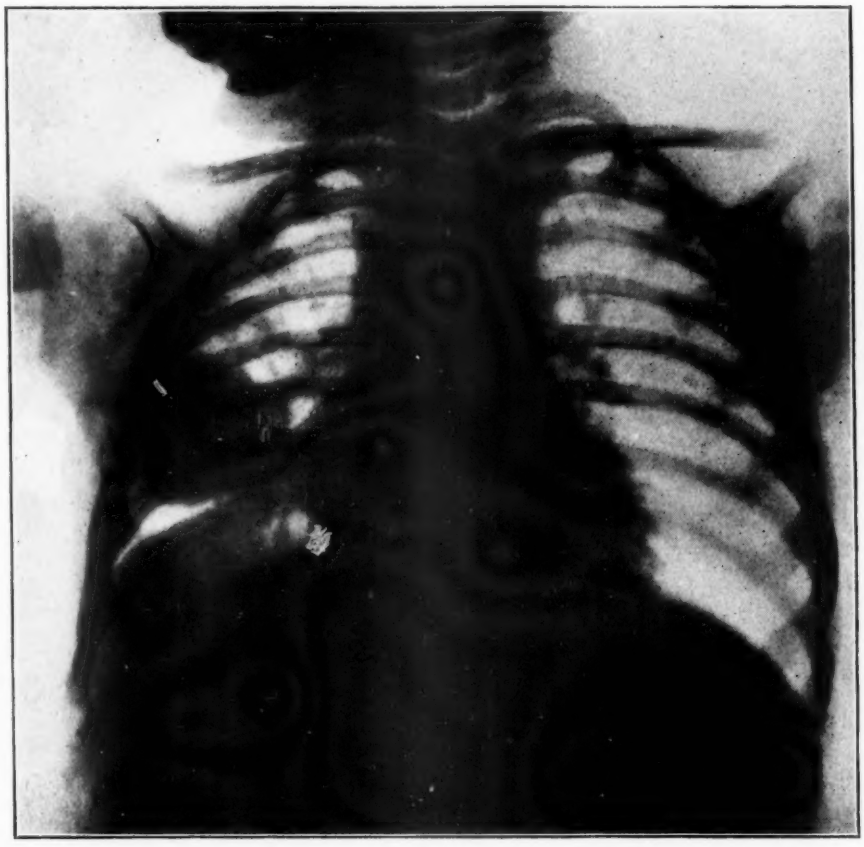

FIG. 4. Case III., L.M. 17/12/27. The area of unresolved pneumonia at the right base is seen. The heart is gradually returning to its normal position, although it is still well to the right side.

Eight days after discharge from hospital to the out-patient department, the child had a relapse which was marked with cyanosis, dyspnœa, a croupy cough and much frothy expectoration. Owing to lack of accommodation, arrangements were made for his admission to the East London Hospital for Children, where he was placed under the care of Dr. G. Bourne, by whose courtesy we were subsequently permitted to examine the child, and who supplied us with the following notes of the case with permission to report them.

28/12/27. The percussion note at the right base is impaired: bronchial breath sounds heard at this area and moist sounds throughout both lungs. The heart sounds are best heard to the right side of sternum. The area of cardiac dullness cannot be defined.

31/12/27. The dullness and bronchial breath sounds are spreading throughout the whole of the right lung. Moist sounds heard at the left lower lobe.

3/1/28. Laryngeal stridor very marked: apparent collapse of whole of right lung and marked cyanosis.

6/1/28. Child much the same except that the whole of left lung is full of moist sounds. Child died that evening.

Post-mortem Examination. Heart was found to be lying almost entirely to the right of middle line. There was a small effusion (? terminal) in the pericardial sac. The left lung was large, full of air, with some purulent bronchitis at the base and a small abscess at the apex of the lower lobe. Patch of pleurisy over left lower lobe. There was consolidation of the middle and upper lobes of the right lung with complete collapse of the right lower lobe. The trachea was normal.

Case IV. L.P., age 6 years. Four days ago woke up screaming and delirious. For two days remained delirious, and was feverish. Had attacks of screaming with apparent pain in right side. Vomited twice on day of admission.

22/5/28. Child is drowsy but not delirious. Looks excessively ill and has a high temperature and rapid respiration.

No physical signs, but irritability, head retraction and meningism.

23/5/28. Impaired percussion note right apex. Breathing high pitched. No crepitations heard. Apex beat 4th space half-inch internal to nipple line, sounds normal. Tonsils unhealthy. Naso-pharyngeal discharge. No other physical signs, and head retraction is now absent. Cerebro-spinal fluid normal. Wassermann reaction negative.

X-ray shows an increase in density of right upper lobe, with displacement of heart to right.

31/5/28. No high pitched breath sounds, but some impairment of percussion note right upper lobe, and on deep breathing and coughing crepitations are heard at bases, and also at right lower lobe. Looks better. Temperature and respiration settling to normal. Area of cardiac dullness does not extend to right, but apex beat still internal to nipple.

4/6/28. X-ray shows the whole of the right chest to be less translucent than the left. The upper part of the right upper lobe appears clearer; the lower part is mottled. The right lower lobe seems slightly involved now. The left chest is clear. The heart and trachea are still to the right, their position being similar to that noted on 24/5/28.

7/6/28. Chest seems clear now. Heart normal in position.

11/6/28. The temperature and respiration rate have been normal for two weeks and the child seems quite well.

Case V. J.R., age 10 months. There is a strong family history of tuberculosis on the father's side. 11 days ago child was taken ill and diagnosed as having pneumonia, by private practitioner. For the past week he has had a high temperature with cough, and has been vomiting frequently.

26/9/28. High pitched breath sounds noted over the left lower lobe, but no other definite physical signs. Heart appears normal in position.

6/10/28. The respiration rate is raised and the temperature high and swinging. The breath sounds at the left base are diminished, otherwise nothing is to be noted. On account of the swinging temperature left lung explored by needle. No definite pus obtained. A catheter specimen of urine, acid in reaction, contained a trace of albumin, a few leucocytes and epithelial cells; from it B. coli and proteus cultured. Von Pirquet reaction negative. Stomach washings fail to reveal tubercle bacilli.

16/10/28. X-ray shows density over left base with heart and trachea slightly to right. Left diaphragm does not show up under screen. Slightly increased density right lower lobe (Fig. 5). As a result of the X-ray left base was again needled with a negative result. The temperature and respiration rate are now normal.

28/10/28. The child, who has been discharged, has attended as an out-patient, and physical examination shows diminished breath sounds both right and left bases, with hyper-resonance at right upper lobe and heart displaced markedly to the right.

29/10/28. X-ray now shows wedge-shaped area of consolidation at right base, left base being clear. There is no evidence of pneumothorax. The heart is well over to the right (Fig. 6).

31/10/28. Cough is marked, temperature raised. Physical examination shows left base clear. Hyper-resonance left axillary region and over præcordial area. Impaired percussion note and diminished breath sounds at right base. Area of cardiac dullness not defined owing to hyper-resonance over præcordium (emphysema). Apex beat felt and heard loudest just to left edge of sternum. Child re-admitted to hospital.

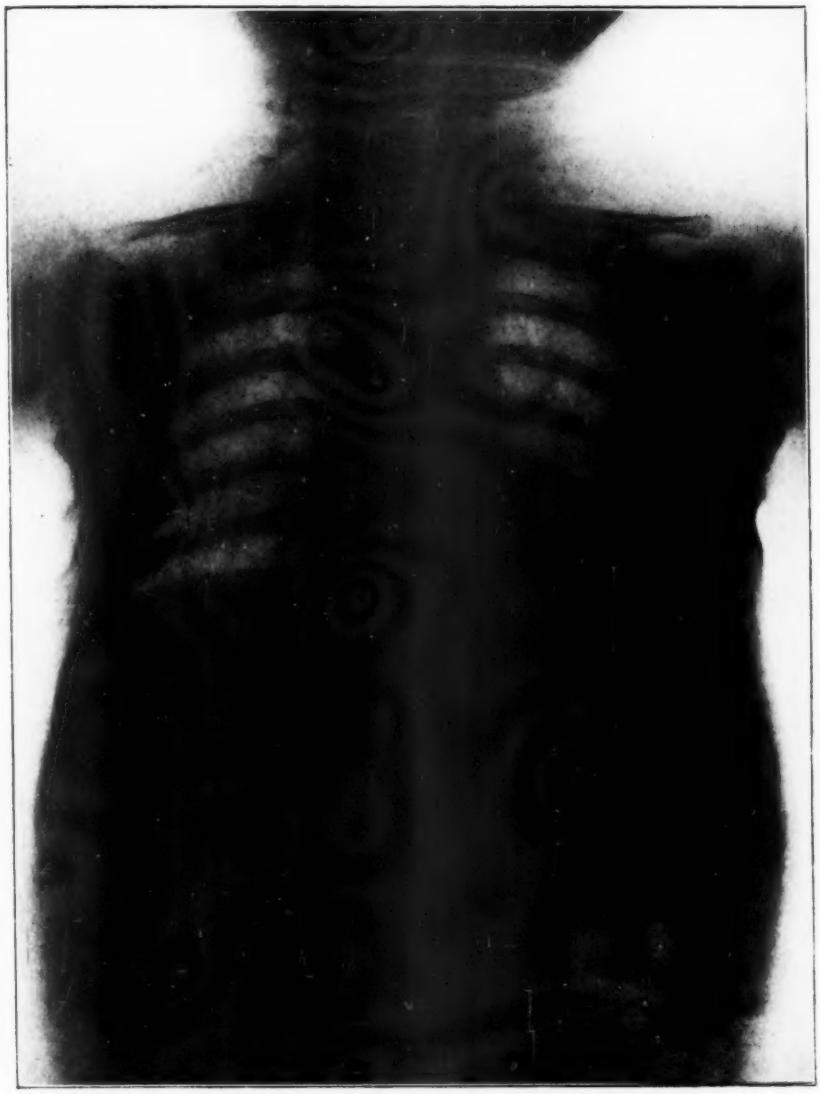

FIG. 5. Case V., J.R. 15/10/28. The heart and trachea are slightly displaced to the right side, and there is slight increase in density at the right lower lobe. The left lower chest is dull and a diagnosis of fluid at the left base was made, but no fluid was obtained on needling.

5/11/28. Temperature and respiration, which have both been raised, now fallen to normal.

9/11/28. Temperature remains steady and normal. Child seems well. Impaired percussion note at right base, otherwise no physical signs in lungs. Heart going back to normal position, the apex beat now being half-inch internal to nipple line.

20/2/29. Since last seen child has been ill with an exacerbation of the previous condition For two months has been receiving artificial sunlight treatment, and now looks in good health, and is said to be very well. No physical signs in lungs. Apex beat of heart ¼-inch internal to nipple line.

X-ray shows the heart normal in size, shape, and position; the trachea is slightly to the right side, and there is some slight increase of density at the lower part of the right upper lobe which is probably largely due to inter-lobar thickening. This would explain the fact that the trachea is not in the mid-line.

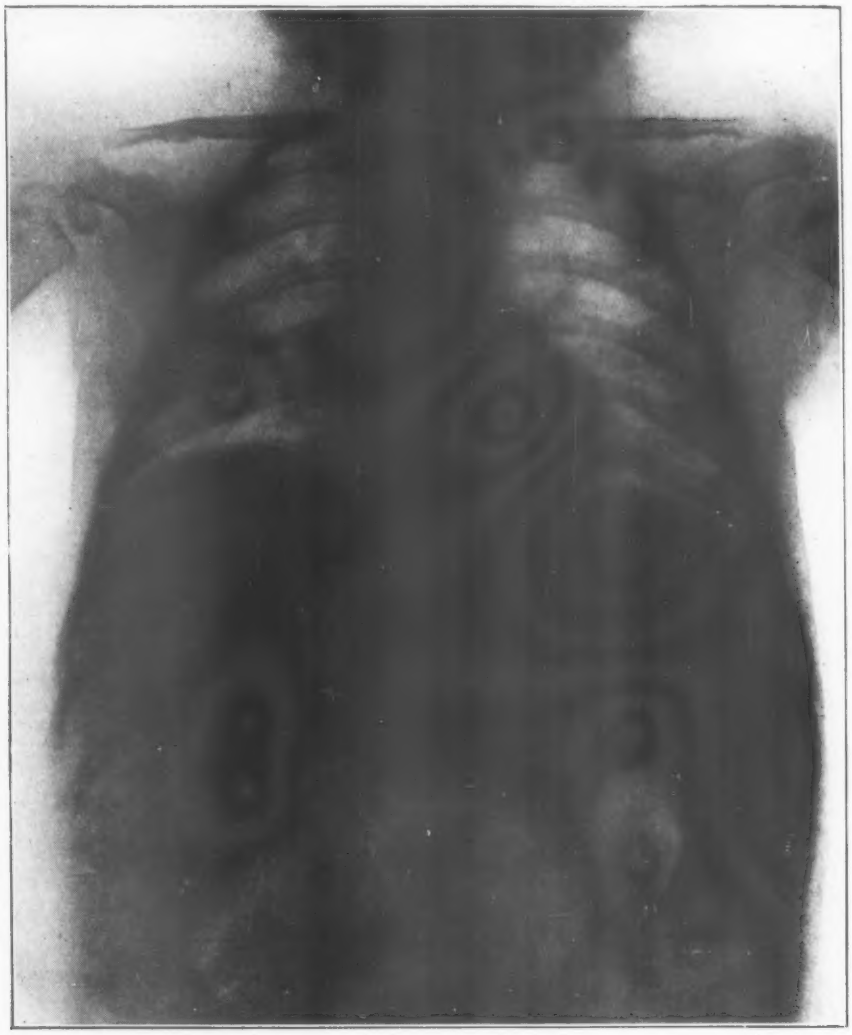

FIG 6. Case V., J.R. 29/10/28. The left base is now clear, and no pneumo-thorax is seen. The heart is still well displaced to the right. There is a local area of pneumonia at the right lower lobe.

DISCUSSION.

It is by no means easy in every case of pneumonia to make a clear cut diagnosis of its type, whether it be lobar or broncho-pneumonia. Somerville[6] in a recent paper shows that by far the greater number of cases of pneumonia,

occurring in children under 6 years of age are, on a basis of pathological examinations carried out post-mortem, broncho-pneumonic in type. Certainly this is the case in infants. This observer thinks that pathological examination is the only true criterion of the type of disease that has occurred. As criteria of the type of pneumonia present in our cases, the history, physical signs, and course of the disease have all been taken into account rather than the physical signs alone. Considered thus, three of our cases appear to be broncho-pneumonic in type (Cases I, II and III) and two (Cases IV and V) appear to be cases of true lobar pneumonia.

In Case V first the left and subsequently the right side was affected. During the first attack, the heart did not appear to deviate towards the affected side, but when the right lung was affected, the heart showed definite displacement. In four of the cases (Cases I, II, III and IV) the right lung was chiefly affected, the heart deviating towards that side.

Definite emphysema was noted on the side unaffected by pneumonia in two cases (Cases II and V), and in one case where the right side gave evidence of pneumonia, the area of cardiac dullness could not be defined by percussion (Case I). The X-ray photographs reproduced are those which best exemplify the conditions under discussion.

Summary and Conclusions.

Five cases are described in which during an attack of pneumonia, the heart deviated towards the side of the lesion, subsequently returning slowly to a normal position as recovery occurred.

A consideration of these cases and of other similar cases reported in the literature, points to the fact that this phenomenon is not infrequent in childhood, and would in all probability be more often noted if specially looked for by physical examination, and if radiograms of the chest were taken early. Displacement of the heart appears to be brought about by the traction exercised by shrinkage due to partial collapse of the affected lung, aided by the push of the sound lung which is frequently distended by compensatory emphysema.

This cardiac displacement is not caused by a pulling over due to fibrosis, since it occurs in the acute stage of the disease, and the heart subsequently returns to its normal position. Moreover, neither by physical nor by radiological examination can evidence of fibrosis be noted.

We wish to thank Dr. Maitland-Jones for permission to report these cases, which were admitted to the Hospital under his care.

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PAROXYSMAL SNEEZING IN WHOOPING COUGH.

BY

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and

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"He sneezed so hard with the whooping-cough" (Polly-wolly-doodle).

In a 'Treatise on the History, Nature and Treatment of Chincough,' by Dr. Robert Watt of Glasgow, published in 1813, it is mentioned that whooping cough may not only begin like a common cold but sometimes continue in this form throughout the course of the disease. Dr. Watt appeared to be well acquainted with this variation in the normal course of pertussis and he quotes Dr. Cullen as saying, 'I have had instances of a disease which, though evidently arising from the Chincough contagion, never put on any other form than that of a common catarrh.' It is somewhat remarkable in view of these observations that the occurrence of paroxysmal sneezing in whooping cough should be so rare and almost unknown to the present generation of children's physicians. The following case was recently under the care of Dr. Robert Hutchison at the Hospital for Sick Children, Great Ormond Street.

Doreen T., aged 3 years and 11 months, began to whoop in January, 1929. She was very sick with the cough, bringing up nearly everything she ate. This condition lasted until the beginning of March, when she ceased whooping and began to sneeze instead. These sneezing attacks occurred about ten times a day, and each attack caused great distress and incontinence of urine. She had suffered from these attacks for three weeks when she was admitted to hospital with an extensive broncho-pneumonia, severe emaciation and a palpable spleen. While under observation she continued to have paroxysms of sneezing, but did not cough or whoop. The paroxysms consisted of a rapid series of 'expiratory sneezes' resulting in the expulsion through the nose of large quantities of tenacious muco-pus. At the end of the paroxysm she drew in her breath and lay back cyanosed and very exhausted. Sometimes she would lean forward during the attack and sometimes she would get on to her hands and knees. Occasionally vomiting of phlegm would occur after the paroxysm, and the sneezing was often brought on by a drink or by examination of the fauces with a spatula. Three weeks after admission the broncho-pneumonia disappeared while paroxysms of sneezing continued three to twelve times a day. At this time a slight whoop was heard at the end of a paroxysm, and she now began to have both whooping and sneezing attacks. At the end of six weeks the whoop had disappeared although occasional mild sneezing attacks continued.

Bacteriological examination of the muco-pus discharged from the nose in one of the paroxysms demonstrated the presence of Gram-negative bacilli of the pertussis type.

There is one other child in the family and he had pertussis after his sister with the ordinary paroxysms of coughing.

The literature on this rare condition is necessarily scanty, although there is a passing reference to it in the writings of Trousseau, Hutinel, Henoch, and Kassovitz, and more recently in those of also Griffiths and Mitchell, and J. D. Rolleston. In 1883 H. Roger in his 'Recherches cliniques sur les maladies des enfances,' stated that he had seen several children in whom, in place of a cough, paroxysms of sneezing occurred at regular intervals and large quantities

of muco-pus were poured down the nose. Szegö[1] appears to have published the first paper on this subject entitled 'Observations on a form of spasmodic sneezing in whooping cough.' He describes a case of pertussis in which paroxysms of sneezing occurred, while a younger child in the same family had the ordinary form of the disease. He gives a very accurate description of the sneezing attacks, and concludes that such attacks strongly suggest that the spasmodic features of pertussis are central in origin. Seitz[2] mentions the occurrence of sneezing especially in younger children. Dansac[3] in a paper on the atypical forms of whooping cough gives some attention to the occurrence of sneezing. He points out that the cough in pertussis may be replaced not only by sneezing but also by attacks of hiccough. He quotes various authorities who hold that this form is commoner in young children. One important point arises out of Dansac's paper, namely, that an adult with a troublesome and intractable coryza may really be suffering from pertussis and may infect children, and a case of this kind is quoted. Meyer and Burghard[4] have also observed paroxysmal sneezing as an infrequent symptom in 1,064 cases of pertussis under their care. Among other 'equivalents of the whoop' they mention paroxysmal yawning. Reichle[5] has recently described two cases of paroxysmal sneezing in whooping cough, and he lays stress on the fact that sneezing of a paroxysmal character only occurs in one other disorder, namely hay-fever, so that if this can be excluded the occurrence of this rare symptom may sometimes help in diagnosis.

Several points of interest arise in connection with this curious phenomenon, but in the limits of this short note further discussion is not possible. The points raised may be conveniently grouped under the following conclusions :—

(1) Various equivalents of the whoop in pertussis have been described including paroxysmal sneezing. The occurrence of these equivalents seems to point to a central nervous origin for the spasmodic phenomena of pertussis.

(2) Pertussis taking the form of a persistent, unusually severe coryza may not be diagnosed, and such a case may spread the disease.

We are indebted to Dr. Robert Hutchison for permission to publish this case.

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BRITISH PÆDIATRIC ASSOCIATION.

PROCEEDINGS OF THE SECOND ANNUAL GENERAL MEETING.

The Second Annual General Meeting was held at The Palace Hotel, Buxton, on Friday and Saturday, April 26th and 27th, 1929.

FIRST SESSION (APRIL 26TH, 10 A.M.).

Business Proceedings: The President, Dr. Edmund Cautley, was in the Chair, and there were present 43 members and 7 guests.

President: Dr. H. Morley Fletcher was elected President for 1929-30, and the election of Officers, Honorary and Ordinary Members followed, as recommended by the Executive Committee.

Secretary: Dr. Donald Paterson (re-elected).

Treasurer: Dr. H. Morley Fletcher (re-elected).

Representative for London: Dr. Robert Hutchison.

Representative for Scotland: Dr. Charles McNeil.

Honorary Members: Dr. A. Blackader of Montreal and Dr. George Sutherland of London.

Ordinary Members: Drs. J. Murray Bligh (Liverpool), R. D. Clarkson (Larbert), C. F. Harris (London), W. P. H. Sheldon (London) and Kenneth Tallerman (London).

Next Meeting: The place of next year's meeting was discussed and it was decided that it should be held at Harrogate, Blackpool or Scarborough.

Treasurer's Report: Dr. Morley Fletcher presented the Treasurer's Annual Report, which was adopted. This showed a balance of £13 14s. 3d.

Scientific Business.

1. DR. LEWIS H. F. THATCHER (Edinburgh): "Acid Milk Feeding." He discussed the use of acidified skimmed milk in the treatment of feeble infants, and in conditions of dyspepsia where the tolerance for food was low. He had found that whole acidified milk, as originally advocated by Marriott, was very often not tolerated where failure had followed the feeding of ordinary milk mixtures, and he preferred to begin with diluted acidified skimmed milk, working up to undiluted, before adding any extra carbohydrate, usually in the form of dextrimaltose. The milk is allowed to stand for six hours before being skimmed, and is then acidified with B.P. lactic acid, in the proportion of sixty drops to the pint, without being boiled; fat content was found to be round about 1.5%. In this way a fresh food was given with a full protein and a low fat content; moreover, the casein was altered to a fine precipitate of casein lactate, and the food was of a reasonable buffer value, both conditions that ought to render peptic digestion of the essential protein easier.

2. DR. C. PAGET LAPAGE (Manchester): "Recurrent attacks of butyric acidity (sour-sickness in babies) in pyloric spasm and pyloric stenosis." He drew attention to the periodic occurrence of spells of sour-sickness in babies with pyloric delay, either from pyloric spasm or pyloric stenosis. X-ray findings had confirmed this delay. In a spell of sour-sickness the baby was not necessarily very ill, but became languid and tired, lost appetite, and either posseted or vomited very sour smelling fluid. The smell was due to butyric acid. Overfeeding, especially on fats, might predispose, but the attacks might occur on any food. He said that precautions should be taken to guard against these attacks by giving grey powder or rhubarb and soda, and by limiting the fats.

3. DR. H. T. ASHBY (Manchester): "Acute anaphylaxis to cow's milk protein in the infant and its treatment." He described a breast-fed infant, who, when given a feed of cow's milk for the first time, had an acute anaphylactic shock. There was swelling of the face, lips and mouth. The infant was much distressed and nearly died. Various skin tests proved that the infant was extremely sensitive to milk of all kinds, egg albumen, soups made from meat, malt, etc. The infant was very gradually desensitized by giving at first minute doses of cow's milk each day and then slowly increasing the amount of milk.

4. Dr. Eric Pritchard (London): "The treatment of pyloric stenosis." He gave a short account of a clinical method for estimating the degree of alkalosis in infants from whom only a small amount of blood could be obtained. The method employed was Payne's modification of Van Slyke, Stillman and Cullens, requiring only 0.05 c. cm. of blood plasm. No other reliable method was at present available. He said it was thought that the sudden collapses which occurred in pyloric cases might in some way be dependent on high degrees of alkalosis. The investigation showed that varying degrees of alkalosis always existed in cases of pyloric obstruction, and that the indication for treatment was the administration of sodium, ammonium, or calcium chloride, and that there was danger in increasing the alkalosis by giving bicarbonate of soda.

5. Dr. Thursfield (London): "Chronic hæmaturia ending in uræmia." He related the case of a boy who suffered from intermittent painless hæmaturia from the age of 3½ years. For several years there were no other symptoms, and at an operation done for suspected stone in the right kidney in 1922 the kidney was reported normal. From 1925 onwards his blood pressure was above the normal, but he enjoyed good health and was fully up to the average in weight and development, playing all school games up to within a week of his death from uræmia. The kidneys were finely granular, and showed microscopically diffuse interstitial and glomerular changes.

6. Dr. Robert Hutchison (London): "Paroxysmal sneezing in whooping cough." He described a case in which the patient, a girl of 4, was admitted for extensive broncho-pneumonia. Five weeks previously she had begun to whoop, but after three weeks the paroxysms of cough had given place to paroxysmal sneezing. The attacks were very striking and recurred from 8 to 10 times in the 24 hours. They consisted in a succession of violent sneezes—perhaps 6 or 7—during which the child became black in the face and after which she was rather collapsed for a time. During the sneezing a very large quantity of thick muco-purulent material was discharged from the nose and this was found to contain Bordet's bacillus. After the child had been a fortnight in hospital the sneezing became less frequent and was partly replaced by the usual paroxysms of cough.

7. Dr. D. N. Nabarro (London): "The present incidence of dysentery in this country." He said that at Great Ormond Street, in the year 1928, there were 15 cases of bacteriological dysentery (that is, cases in which one or other of the typical dysentery bacilli was isolated); 13 of these were due to the Sonne bacillus and 2 to the Flexner. There were two deaths, one with each bacillus. During the first four months of 1929 there had been in all 13 cases, with 5 deaths; of these 9 were due to the Sonne bacillus, with 4 deaths, and 4 to the Flexner bacillus with one death. Several points of interest were brought out by recent small outbreaks: (1) that the Sonne bacillus might be the cause of a fatal dysentery (this was not a new observation, but was often not realised); (2) that some of the very young children died very quickly, within 24 hours of being affected; and (3) post mortem the lesions found in the intestine might be either very slight ulceration or sometimes even only a general reddening of the bowel wall.

8. Dr. E. Bellingham Smith (London): "An attack of dysentery of unusual type." He commented on a recent epidemic of dysentery at the Queen's Hospital for Children, various names having been given to the organism. He thought ulcerative colitis in older people was probably chronic dysentery.

9. Dr. Robert Marshall (Belfast): "Brachydactyly in a child, its mother and aunt." He described a child aged one year, whose mother, aunt, uncle, and, it was said, maternal grandmother and great-grandmother were similarly affected. The condition was interesting in view of Bateson's statement that it was the first condition in man found to obey Mendelian laws of heredity. The brachydactyly was of the type in which there is apparent absence of the middle phalanx in both fingers and toes. Photographs and radiograms were shown.

Second Session (April 26th, 8.30 p.m.).

10. Dr. Bernard Schlesinger (London): "The treatment of chorea by nirvanol." He stated that this drug, phenylethylhydantoin, had received an extensive trial in Germany, but had not as yet been used in this country. He had treated four cases of chorea by this method with such favourable results that he proposed to extend the use of the drug to other types of

rheumatism. He then gave details of its mode of action, the effect on the blood count, and showed charts illustrating the various points. He also mentioned certain adverse effects of the drug that had occasionally been known to occur and suggested possible methods of avoiding them.

11. Dr. Charles McNeil (Edinburgh): "Different types of bronchiectasis in children." He gave clinical notes in four cases of bronchiectasis in children, illustrated by lipiodol X-ray photographs. In all there was a fairly good state of general health, associated with typical clinical features. Two showed a limited bilateral bronchiectasis, of saccular type in one instance, and cylindrical in the other. The remaining two were examples of extensive unilateral bronchiectasis combined with fibroid contraction of the lung.

12. Dr. C. Wilfred Vining (Leeds): "Some remarks concerning pneumonia of infancy, with special reference to the subcutaneous administration of oxygen." He referred to a series of 147 cases with a mortality of 47%. 48 of the cases were admitted from households where influenza was prevalent. Oxygen had been given subcutaneously in all the cases, approximately 60 c.cm. being administered into the soft tissues of the thigh twice daily. While in no case in his experience had it done harm locally or generally, yet he had seen nothing in the results to justify him in believing that anything was gained by giving oxygen in this way. He recorded his opinion that the alkaloids of belladonna were definitely useful, especially in the generalized type of case with cyanosis, but no massive consolidation. He also expressed the opinion that lobar pneumonia did occur during the first three years of life, although he agreed that its differentiation from broncho-pneumonia was not always possible by the physical signs alone.

13. Dr. W. A. Alexander (Edinburgh): "Remarks on slowly-resolving pneumonia in children." He referred to a group of 45 cases (under the charge of Dr. McNeil) in which a localized pneumonia, after persisting for weeks or months, had eventually cleared up with little or no evidence of permanent damage to lung structure. The incidence in a large pneumonia series was 7%, and the age in more than half was 3 years or over. No case in which pus had been detected had been included, but it was the opinion of many that delayed resolution simply meant an undiscovered empyema. None of the cases seemed to fit in with the conception of epituberculosis. In a few hypothyroidism was evident. The initial pneumonia seemed usually to be of lobar type, but it was likely that the inflammatory process had affected the pulmonary stroma to a degree unusual in lobar pneumonia, and that recovery was seldom so complete as it seemed.

14. Dr. E. Bellingham Smith (London): "Extensive surgical emphysema in a case of broncho-pneumonia."

15. Dr. H. Morley Fletcher (London): "Subcutaneous emphysema in children." He related a case of subcutaneous emphysema in a healthy boy of three. On January 11th, he had a slight cough. At 3 p.m. he vomited, his temperature was 100°, he had a short dry cough and his lungs were natural. At 7 p.m. his neck was swollen and he had subcutaneous emphysema. On January 12th, the temperature was 101°, and the emphysema had extended over the face and the whole of the trunk and upper arms. The child presented an extraordinary blown-out appearance, the eyes being completely closed. The breath sounds were inaudible owing to the subcutaneous emphysema. The temperature fell in a few days and the emphysema gradually subsided, the child making a complete recovery. The chief feature of the case was the rapid onset without dyspnœa or definite signs of broncho-pneumonia. This suggested rupture of a tuberculous gland in the bronchus, but the favourable termination negatived this diagnosis.

16. Dr. Hector Cameron (London): "Trismus neonatorum." He said that the so-called tetanus neonatorum was not due to the specific tetanus bacillus, but was a manifestation of a generalized sepsis. Formerly the disease had been extremely common in the country under the name of 'eight-day fits' or trismus or tetanus neonatorum. Up to 1780 17% of the infants born in the Rotunda succumbed. With improved hygiene the death rate rapidly declined, persisting only in the most primitive parts of the country, as in St. Kilda. To-day it was still rife in India and in the West Indies. In 1884 a few months before the discovery of the tetanus bacillus, Hartigan published a careful post-mortem study of 23 cases, in most of which there was evidence of the extravasation of lymph or serum around the spinal cord. With the discovery of the tetanus bacillus it was assumed that trismus was due to tetanus. Photographs of cases of trismus were shown, in which search for the tetanus bacillus had proved negative, but from

which cerebro-spinal fluid had been removed, showing a high protein content and a great increase of cells. The spasm of the jaw in trismus was generally less persistent than the spasm of hands and feet. In one case after death infective endocarditis was found.

17. Dr. J. S. Y. Rogers (Dundee): "A case of diaphragmatic hernia." He described a child aged 7 months, suffering from broncho-pneumonia. The bulk of the liver seemed in the left side, the heart was in a normal position, the spleen on the left side, low down in the pelvis. It was diagnosed as congenital diaphragmatic hernia. The X-ray was difficult to read but an abnormal shadow in left chest was suggestive of diaphragmatic hernia of the liver. No barium was seen in the chest after a barium meal. Post mortem a hernia of the liver through the left sterno-costal hiatus, where the superior epigastric vessels perforate the diaphragm, was seen. The sac had a peritoneal covering and was therefore a true hernia. The liver was altered in shape and was embryonic in type in that both halves were equal and were lobulated. There was also a groove where the liver was constricted by the neck of the sac. The hernia was at an uncommon site and contained the liver only, the liver alone being a rare hernial content. Of other abnormalities present, the left kidney was congenitally absent, the left suprarenal was present with a vein running direct into the inferior vena cava, the ductus venosus was patent and opened into the right auricle and the spleen was displaced into the pelvis.

Third Session (April 27th, 10 a.m.).

18. Dr. C. W. Vining, with Dr. H. H. Moll (Leeds): "The Pink Disease with special reference to the neurological findings in a series of fatal cases." These findings are to be published in full at an early date.

19. Dr. Norman Capon (Liverpool): "Idiopathic hypertrophy of the heart." He described an example of cardiac hypertrophy and dilatation in a male child four months old. The infant was extremely ill when first seen and the clinical findings were suggestive of left-sided pneumonia, with pericardial effusion. Autopsy showed a heart more than three times the normal size; the left coronary artery was found to arise from the pulmonary artery and there was possibly a slight grade of infantile coarctation. The blood supply of the myocardium under these abnormal conditions was discussed, and references were made to somewhat similar cases reported in the literature.

20. Dr. E. W. Neill Hobhouse (London): "A case of spinal birth injury." He described the case of a child 4 months old when first seen, who was said to be unable to use the right arm. The confinement was difficult and prolonged, breech presentation. During the first weeks neither arm was moved, but during the second and third months the left arm developed movements and then the right hand. When first seen there were movements in the right hand and forearm, but flaccid paralysis of the deltoid, shoulder girdle and triceps. There was slight rigidity in the legs, and sensation was somewhat diminished. The arm was splinted in abduction; active movement developed first in the triceps and then in all the other muscles. The case was in all probability one of hæmatomyelia occasioned by traction on the breech, similar to the cases described by Crothers and Putnam in their monograph on spinal birth injuries.

21. Dr. E. Bellingham Smith (London): "Three cases of thallium acetate poisoning." He described a boy aged 9, a girl aged 7 and a boy aged 4, who had been given thallium acetate for ringworm. By some mistake they were given three doses instead of the usual one. The elder boy, who had had two doses, got severe pains in his legs, but after showing great weakness, recovered in one week. The younger boy, who had had three doses, but had vomited the last, was weaker and could not stand. He recovered in six weeks. The girl, who retained all her three doses, was unconscious and had flaccid paralysis remaining so for 3 days, then became conscious and developed movement, with groaning, mental irritation, screaming and blindness. About a month after the reflexes appeared, but she was still blind and incontinent. A fortnight later she had tremors of the face and jaw and hands with hyperæsthesia. She was given nasal feeds and subcutaneous salines. She had insomnia and a rapid pulse. This continued for a further three months, then she began to improve, to speak and to hear and see. Five months later she could just stand alone, and after another two months walked and talked intelligently. She was at present intelligent, but could not see well. She could read but still had a very ataxic gait. The speaker suggested that the children had an acute encephalitis, like lead poisoning.

22. Dr. L. G. Parsons with Dr. K. D. Wilkinson (Birmingham): "Osteosclerosis Fragilis (Albers-Schomberg disease)."

23. Dr. L. G. Parsons (Birmingham): "Three cases of pellagra in one family." He described a family of four daughters, of respectable parents, living 12 miles from Birmingham 300 feet above a river. The eldest girl of 12 was quite well. All the children were breastfed until nine months old. The second child had a rash on her legs at 16 months and died. The third child became ill at 10 months old, had diarrhœa and vomiting, spasmodic movements and spastic legs. At 2 years and 5 months she was admitted to Hospital, but died 24 hours after. The face was expressionless, there was no rash, but there were fine tremors of the hands. The lumbar puncture was normal, and nothing was found post mortem. The fourth child came under observation at 2 years with a rash. Six months later she came into hospital with a rash, desquamation and incipient convulsions and spasticity. Vitamin B was given, and she improved greatly and at present seemed a normal child.

24. Dr. F. J. Poynton (London): "A case of (?) Renal Teratoma." This case was described by Dr. Moncrieff in the absence of Dr. Poynton. A girl aged one year and six months was noticed to have a swelling in the left side of her abdomen since the age of six months, with no urinary or other symptoms except some abdominal tenderness of a week's duration. On examination there was a cystic swelling in the position of the left kidney and a ureteric catheter would not pass up the left ureter. Operations showed a large mass attached to the left kidney which was completely removed. The mass proved to be a cyst containing warty growths. Microscopic examination showed that this was an adeno-sarcoma of the kidney. The child made a good recovery after operation.

25. Dr. William Brown (Aberdeen): "Congenital hydronephrosis."

26. Dr. Wilkie Scott (Nottingham): "Cases of pneumococcal peritonitis." He described some cases recently under his care. One was an infant of 21 days with purulent peritonitis, in whom there was also pneumonic consolidation of the lungs. He suggested that some cases of so-called primary peritonitis were really cases of pneumococcal septicæmia with concurrent infection of the lungs and peritoneum. He emphasized the difficulty in diagnosis of those cases of primary peritonitis where the early symptoms were diarrhœa and vomiting without abdominal pain or rigidity and asked for suggestions as to the best course to adopt where, with these symptoms, there might be a suspicion of pneumococcal peritonitis.